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=> fil reg
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STRUCTURE FILE UPDATES:   20 MAY 2003  HIGHEST RN 518004-10-9
DICTIONARY FILE UPDATES:  20 MAY 2003  HIGHEST RN 518004-10-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> e bromoquercetin/cn
E1            1     BROMOPYRUVIC ACID ETHYL ESTER/CN
E2            1     BROMOPYRUVOYL CHLORIDE/CN
E3            0 --> BROMOQUERCETIN/CN
E4            1     BROMOREBECCAMYCIN/CN
E5            1     BROMORESERPINE/CN
E6            1     BROMORUTHENOCENE/CN
E7            1     BROMOSAFROLE EPOXIDE/CN
E8            1     BROMOSALICYLANILIDE/CN
E9            1     BROMOSALICYLCHLORANILIDE/CN
E10           1     BROMOSALICYLIC ACID/CN
E11           1     BROMOSALIGENIN/CN
E12           1     BROMOSAN/CN
```

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=> fil DRUGU, PASCAL, BIOSIS, WPIDS, SCISEARCH
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FILE 'WPIDS' ENTERED AT 10:29:46 ON 22 MAY 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE 'SCISEARCH' ENTERED AT 10:29:46 ON 22 MAY 2003
COPYRIGHT 2003 THOMSON ISI
```

inventors

```
=> d que l87; d que l88; s l87 or l88

L1          3270 SEA FILE=CAPLUS ABB=ON  MILLER G?/AU
L2          2750 SEA FILE=CAPLUS ABB=ON  BROWN L?/AU
L81        10125 SEA L1
L82         9326 SEA L2
L86        46071 SEA TOCOPHEROL#
L87            5 SEA L81 AND L82 AND L86



L1          3270 SEA FILE=CAPLUS ABB=ON  MILLER G?/AU
L2          2750 SEA FILE=CAPLUS ABB=ON  BROWN L?/AU
L81        10125 SEA L1
L82         9326 SEA L2
L84       403762 SEA ISCHEMI? OR ISCHAEMI? OR ANTIISCHEMI? OR ANTIISCHAEMI?
L86        46071 SEA TOCOPHEROL#
L88            1 SEA (L81 OR L82) AND L84 AND L86


L106           5 L87 OR L88

=> fil capl; d que l26; d que l28

FILE 'CAPLUS' ENTERED AT 10:29:50 ON 22 MAY 2003
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FILE COVERS 1907 - 22 May 2003  VOL 138 ISS 21
FILE LAST UPDATED: 21 May 2003  (20030521/ED)
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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L1          3270 SEA FILE=CAPLUS ABB=ON  MILLER G?/AU
L2          2750 SEA FILE=CAPLUS ABB=ON  BROWN L?/AU
L5             1 SEA FILE=REGISTRY ABB=ON  .BETA.-TOCOPHEROL/CN
L6             1 SEA FILE=REGISTRY ABB=ON  .DELTA.-TOCOPHEROL/CN
L7             1 SEA FILE=REGISTRY ABB=ON  .GAMMA.-TOCOPHEROL/CN
L8             1 SEA FILE=REGISTRY ABB=ON  CHRYSIN/CN
L9             1 SEA FILE=REGISTRY ABB=ON  DAIDZEIN/CN
L10            1 SEA FILE=REGISTRY ABB=ON  DIOSMIN/CN
L11            1 SEA FILE=REGISTRY ABB=ON  HESPERETIN/CN
L12            1 SEA FILE=REGISTRY ABB=ON  HESPERIDIN/CN
L13            1 SEA FILE=REGISTRY ABB=ON  LUTEOLIN/CN
L14            1 SEA FILE=REGISTRY ABB=ON  QUERCETIN/CN
L15            1 SEA FILE=REGISTRY ABB=ON  RUTIN/CN
L16            1 SEA FILE=REGISTRY ABB=ON  BIOCHANIN/CN
L17         1288 SEA FILE=CAPLUS ABB=ON  L5 OR BETA(A) TOCOPHEROL#/OBI
L18         1521 SEA FILE=CAPLUS ABB=ON  L6 OR DELTA(A) TOCOPHEROL#/OBI
L19         2416 SEA FILE=CAPLUS ABB=ON  L7 OR GAMMA(A) TOCOPHEROL#/OBI
L20        15966 SEA FILE=CAPLUS ABB=ON  (L8 OR L9 OR L10 OR L11 OR L12 OR L13
              OR L14 OR L15 OR L16)
L21        20609 SEA FILE=CAPLUS ABB=ON  FLAVONOIDS/CT OR FLAVONES/CT OR
              ISOFLAVONOIDS/CT
L22         5639 SEA FILE=CAPLUS ABB=ON  ISCHEMIA/CT
L23         3221 SEA FILE=CAPLUS ABB=ON  (ANTI ISCHEMI? OR ANTIISCHEMI?)/OBI
L26            2 SEA FILE=CAPLUS ABB=ON  (L1 OR L2) AND (L22 OR L23) AND (L17
              OR L18 OR L19 OR L20 OR L21)


L1          3270 SEA FILE=CAPLUS ABB=ON  MILLER G?/AU
L2          2750 SEA FILE=CAPLUS ABB=ON  BROWN L?/AU
L22         5639 SEA FILE=CAPLUS ABB=ON  ISCHEMIA/CT
L23         3221 SEA FILE=CAPLUS ABB=ON  (ANTI ISCHEMI? OR ANTIISCHEMI?)/OBI
L28            3 SEA FILE=CAPLUS ABB=ON  L1 AND L2 AND (L22 OR L23)


=> s l26 or l28

L107           3 L26 OR L28

=> fil medl; d que l45; d que l47; d que l48

FILE 'MEDLINE' ENTERED AT 10:29:52 ON 22 MAY 2003

 FILE LAST UPDATED: 21 MAY 2003 (20030521/UP).  FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L38         2507 SEA FILE=MEDLINE ABB=ON  MILLER G?/AU
L39         2391 SEA FILE=MEDLINE ABB=ON  BROWN L?/AU
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L40       277250 SEA FILE=MEDLINE ABB=ON  ISCHEMIA+NT/CT
L41           15 SEA FILE=MEDLINE ABB=ON  TOCOPHEROLS/CT AND DELTA
L42            5 SEA FILE=MEDLINE ABB=ON  BETA-TOCOPHEROL/CT
L43           45 SEA FILE=MEDLINE ABB=ON  GAMMA-TOCOPHEROL/CT
L44          824 SEA FILE=MEDLINE ABB=ON  (BETA OR DELTA OR GAMMA)(A)TOCOPHEROL#

L45            0 SEA FILE=MEDLINE ABB=ON  (L38 OR L39) AND L40 AND (L41 OR L42
                  OR L43 OR L44)



L38         2507 SEA FILE=MEDLINE ABB=ON  MILLER G?/AU
L39         2391 SEA FILE=MEDLINE ABB=ON  BROWN L?/AU
L40       277250 SEA FILE=MEDLINE ABB=ON  ISCHEMIA+NT/CT
L47            0 SEA FILE=MEDLINE ABB=ON  L38 AND L39 AND L40



L38         2507 SEA FILE=MEDLINE ABB=ON  MILLER G?/AU
L39         2391 SEA FILE=MEDLINE ABB=ON  BROWN L?/AU
L41           15 SEA FILE=MEDLINE ABB=ON  TOCOPHEROLS/CT AND DELTA
L42            5 SEA FILE=MEDLINE ABB=ON  BETA-TOCOPHEROL/CT
L43           45 SEA FILE=MEDLINE ABB=ON  GAMMA-TOCOPHEROL/CT
L44          824 SEA FILE=MEDLINE ABB=ON  (BETA OR DELTA OR GAMMA)(A)TOCOPHEROL#

L48            0 SEA FILE=MEDLINE ABB=ON  (L38 OR L39) AND (L41 OR L42 OR L43
                  OR L44)

=> fil embase; d que l72; d que l79

FILE 'EMBASE' ENTERED AT 10:29:53 ON 22 MAY 2003
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L70         1747 SEA FILE=EMBASE ABB=ON  MILLER G?/AU
L71         1713 SEA FILE=EMBASE ABB=ON  BROWN L?/AU
L72            0 SEA FILE=EMBASE ABB=ON  L70 AND L71



L70         1747 SEA FILE=EMBASE ABB=ON  MILLER G?/AU
L71         1713 SEA FILE=EMBASE ABB=ON  BROWN L?/AU
L74          130 SEA FILE=EMBASE ABB=ON  BETA TOCOPHEROL/CT
L75          498 SEA FILE=EMBASE ABB=ON  GAMMA TOCOPHEROL/CT
L76          128 SEA FILE=EMBASE ABB=ON  DELTA TOCOPHEROL/CT
L79            0 SEA FILE=EMBASE ABB=ON  (L70 OR L71) AND (L74 OR L75 OR L76)


=> dup rem l107,l106
FILE 'CAPLUS' ENTERED AT 10:30:13 ON 22 MAY 2003
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FILE 'BIOSIS' ENTERED AT 10:30:13 ON 22 MAY 2003
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FILE 'WPIDS' ENTERED AT 10:30:13 ON 22 MAY 2003

PROCESSING COMPLETED FOR L107
PROCESSING COMPLETED FOR L106
L108 5 DUP REM L107 L106 (3 DUPLICATES REMOVED)
ANSWERS '1-3' FROM FILE CAPLUS
ANSWER '4' FROM FILE BIOSIS
ANSWER '5' FROM FILE WPIDS

=> d ibib ab 1-5

L108 ANSWER 1 OF 5 CAPLUS DUPLICATE 1
ACCESSION NUMBER: 2002:465811 CAPLUS
DOCUMENT NUMBER: 137:28330
TITLE: Compositions and methods for the treatment of tissue ischemia
INVENTOR(S): **Miller, Guy Michael; Brown, Lesley A.**; Del Balzo, Ughetta; Flaim, Stephen; Boddupalli, Sekhar; Wang, Bing
PATENT ASSIGNEE(S): Galileo Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002047680	A2	20020620	WO 2001-US50984	20011214
WO 2002047680	A3	20030327		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002039748	A5	20020624	AU 2002-39748	20011214
US 2002132845	A1	20020919	US 2001-17717	20011214
US 2002143049	A1	20021003	US 2001-20450	20011214

PRIORITY APPLN. INFO.:			
US 2000-256269P	P	20001215	
US 2001-296580P	P	20010606	
US 2001-296581P	P	20010606	
US 2001-343575P	P	20011019	
WO 2001-US50984	W	20011214	

AB The present invention provides compns. and methods for the treatment of tissue ischemia, and in particular, cerebral ischemia. In particular, the present invention provides gamma-, beta-, or delta-tocopherol enriched tocopherol compns. and gamma-, beta, or delta-tocopherol metabolite enriched compns. and/or flavonoid enriched and/or a flavonoid deriv. enriched compns. and methods for their use in preventing or treating a tissue ischemic condition or a cerebral ischemic condition. The present invention also provides pharmaceutical compns. comprising gamma-, beta-, or delta-tocopherol enriched tocopherol compn., a gamma-, beta-, or delta-tocopherol metabolite enriched compns. or flavonoid enriched compns. or flavonoid deriv. enriched compns.

L108 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 2002:570708 CAPLUS
DOCUMENT NUMBER: 137:119700
TITLE: Formulations of tocopherols and methods of making and using them
INVENTOR(S): **Miller, Guy; Brown, Lesley A.**
PATENT ASSIGNEE(S): Galileo Laboratories, Inc., USA
SOURCE: U.S., 28 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6426362	B1	20020730	US 2000-684588	20001006
US 2003022818	A1	20030130	US 2002-188587	20020702

PRIORITY APPLN. INFO.: US 1999-158234P P 19991008
US 2000-684588 A1 20001006

AB Non-naturally-occurring compns. for use in amelioration of disruption of energy metab. secondary to stress are described. The compns. comprise a tocopherol and/or a deriv. thereof, and a synergist, and are particularly suited for use as nutritional supplements. Synergists include, but are not limited to, flavonoids and lactoferrin and/or derivs. thereof. Compns. comprising an optimized formulation comprising a tocopherol and an addnl. compd. such as daidzein or biochanin A are also described. Methods of making these compns. and methods of ameliorating injury(ies) or disruption of energy metab. secondary to stress, comprising administering such compns., are also disclosed. Various concns. of tocopherols and flavonoids were tested in vitro for the combined ability to ameliorate disruption of energy metab. secondary to stress. For example, diosmin (3.3-100 .mu.M) was not protective by itself, but was synergistic in that range with 10 .mu.g/mL (.+-.)-.alpha.-tocopherol, a concn. at which (.+-.)-.alpha.-tocopherol was only slightly (about 15%) protective by itself. The combination of 100 .mu.M diosmin and 100 .mu.g/mL (.+-.)-.alpha.-tocopherol greatly reduced cell death, providing about 70% protection against stress-induced cell death, indicating synergism between these components. A combinations of 100 .mu.M diosmin and 11 .mu.g/mL (.+-.)-.alpha.-tocopherol was also synergistic.

REFERENCE COUNT: 95 THERE ARE 95 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L108 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:97274 CAPLUS
DOCUMENT NUMBER: 138:153318
TITLE: Preparation of substituted phenols as cytoprotective agents useful in pharmaceutical and cosmetic formulations
INVENTOR(S): Wang, Bing; Zhang, Yong-Kang; Chen, Jian; Zhang, Wei; Song, Jiangao; Del, Balzo Ughetta; **Brown, Lesley; Miller, Guy**
PATENT ASSIGNEE(S): Galileo Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 161 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003009807	A2	20030206	WO 2002-US23509	20020723

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003073712 A1 20030417 US 2002-202670 20020723
PRIORITY APPLN. INFO.: US 2001-307439P P 20010723
US 2002-353702P P 20020131

OTHER SOURCE(S): MARPAT 138:153318

AB Phenolic derivs. having conjugated bonds I [wherein R = NO2, substituted alkenyl, or (un)substituted aryl(carbonyl), heteroaryl, or heterocyclyl; R1-R5 = independently H, carboxy, CN, halo, OH, NO2, nitrone, sulfonate, or (un)substituted alkoxy(carbonyl), alkenyl, alkyl, or (hetero)aryl; or 2 adjacent members of R1 to R5 = O- and together complex with C or a metal; provided that at least 1 of R1 to R5 = MeOCH2O or H(CH2CMe=CHCH2)n; n = 1-4; further provided that when R1 to R5 = MeOCH2O, R = Ph para-substituted by CN, NO2, nitroso, NHOH, NH2CO, alkyl ester, N-contg. heterocyclyl, etc.; R6 = H or (un)substituted alkoxycarbonyl; or stereoisomers or pharmaceutically acceptable salts thereof] were prepd. as cytoprotective agents useful in pharmaceutical and cosmetic formulations. For example, coupling of (4-nitrobenzyl)triphenylphosphonium bromide with 3,4-bis(methoxymethoxy)benzaldehyde using LiOEt in EtOH (41%) followed by deetherification with concd. HCl in EtOH gave 4-[2-(4-nitrophenyl)vinyl]benzene-1,2-diol (81%). The latter was among invention compds. that showed significant redn. in edema in assays assessing rat paw edema (10 to 70%, $p < 0.05$) and mouse ear inflammatory response to topical arachidonic acid (15 to 80%, $p < 0.05$). Results from the neuronal cell stress assay and the rat middle cerebral artery occlusion model of cerebral ischemia were also disclosed for selected invention compds. Thus, I are useful in the treatment of certain ischemic or inflammatory conditions, including but not limited to stroke, myocardial infarction, congestive heart failure, and skin disorders characterized by inflammation or oxidative damage.

L108 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2003:172842 BIOSIS
DOCUMENT NUMBER: PREV200300172842
TITLE: Compositions of flavonoids for use as cytoprotectants and methods of making and using them.
AUTHOR(S): **Brown, Lesley A.; Miller, Guy**
ASSIGNEE: Galileo Laboratories, Inc.
PATENT INFORMATION: US 6528042 March 04, 2003
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar. 4 2003) Vol. 1268, No. 1, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English

AB Non-naturally-occurring compositions for use in amelioration of disruption of energy metabolism secondary to stress are described. These compositions comprise a flavonoid or derivative thereof and a synergist. Synergists include, but are not limited to, amino acids, carbohydrates, carnitines, flavonoids, nucleosides, and **tocopherols** and/or derivatives thereof. Methods of making these compositions and methods of ameliorating disruption of energy metabolism secondary to stress, comprising administering such synergistic compositions, are also disclosed.

L108 ANSWER 5 OF 5 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2003-278496 [27] WPIDS
DOC. NO. CPI: C2003-072827
TITLE: Use of non-alpha **tocopherols** and their metabolites for reducing levels of inflammatory markers and thus ameliorating the symptoms of inflammation.
DERWENT CLASS: B02 C02
INVENTOR(S): BEINLICH, P; BODDUPALLI, S; **BROWN, L**; DREON, D M; FLAIM, S; **MILLER, G**; PHINNEY, S D
PATENT ASSIGNEE(S): (GALI-N) GALILEO LAB INC
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003015494	A2	20030227	(200327)*	EN	32

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003015494	A2	WO 2002-US26920	20020821

PRIORITY APPLN. INFO: US 2001-314257P 20010821; US 2001-314223P 20010821; US 2001-314256P 20010821

AB WO2003015494 A UPAB: 20030429
NOVELTY - Reducing the level of an inflammatory marker, especially C-reactive protein (CRP), in an individual subject to an inflammatory condition comprises administering a non-alpha **tocopherol** or non-alpha **tocopherol** metabolite enriched **tocopherol** composition.

USE - The method is used to reduce one or more biochemical markers of inflammation, thereby reducing or ameliorating the symptoms of inflammation associated with disease and disorders including cardiovascular diseases or disorders (including atrial fibrillation, unstable angina, coronary artery disease, peripheral artery disease and cardiac allograft vaculopathy), mastitis, pre-eclampsia, inflammatory bowel conditions, stroke, tissue infarction, lumbosciatica, estrogen/progestin hormone replacement therapy, infection (bacterial, viral or protozoal), bacterial meningitis, trauma, surgery, biomaterial implants, smoking, obesity, neurodegenerative diseases (e.g. Alzheimer's), infectious disease (sic) (e.g. myocarditis, cardiomyopathy, acute endocarditis or pericarditis), atherosclerosis, systemic inflammatory response syndrome/sepsis, adult respiratory distress syndrome, asthma, rheumatoid arthritis, osteoarthritis, systemic lupus erythematosus, airway hyper-responsiveness, bronchial hyper-reactivity, chronic obstructive pulmonary disease, congestive heart failure, inflammatory complication of diabetes type I and II, metabolic syndrome, end-stage renal disease, pre-menstrual syndrome or muscle fatigue or inflammation, multiple organ dysfunction syndrome, aging, acute allergic reactions, gingivitis and dermal conditions.

ADVANTAGE - Reduction of inflammatory markers improves prognosis and reduces mortality related to inflammatory diseases.
Dwg.0/0

intentionally
blank

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=> fil capl; d que 129
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FILE COVERS 1907 - 22 May 2003  VOL 138 ISS 21
FILE LAST UPDATED: 21 May 2003  (20030521/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
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text

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L5            1 SEA FILE=REGISTRY ABB=ON  .BETA.-TOCOPHEROL/CN
L6            1 SEA FILE=REGISTRY ABB=ON  .DELTA.-TOCOPHEROL/CN
L7            1 SEA FILE=REGISTRY ABB=ON  .GAMMA.-TOCOPHEROL/CN
L17        1288 SEA FILE=CAPLUS ABB=ON  L5 OR BETA(A) TOCOPHEROL#/OBI
L18        1521 SEA FILE=CAPLUS ABB=ON  L6 OR DELTA(A) TOCOPHEROL#/OBI
L19        2416 SEA FILE=CAPLUS ABB=ON  L7 OR GAMMA(A) TOCOPHEROL#/OBI
L22        5639 SEA FILE=CAPLUS ABB=ON  ISCHEMIA/CT
L23        3221 SEA FILE=CAPLUS ABB=ON  (ANTI ISCHEMI? OR ANTIISCHEMI?)/OBI
L29           4 SEA FILE=CAPLUS ABB=ON  (L17 OR L18 OR L19) AND (L22 OR L23)

=> s 129 not l107
L109          2 L29 NOT L107
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printed w/ inventor search

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=> fil medl; d que l53; d que l54; d que l55; d que l57; d que l69

FILE 'MEDLINE' ENTERED AT 10:31:45 ON 22 MAY 2003

 FILE LAST UPDATED: 21 MAY 2003 (20030521/UP).  FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L40       277250 SEA FILE=MEDLINE ABB=ON  ISCHEMIA+NT/CT
L42            5 SEA FILE=MEDLINE ABB=ON  BETA-TOCOPHEROL/CT
L53            0 SEA FILE=MEDLINE ABB=ON  L40 AND L42
```

```
L40      277250 SEA FILE=MEDLINE ABB=ON  ISCHEMIA+NT/CT
L43          45 SEA FILE=MEDLINE ABB=ON  GAMMA-TOCOPHEROL/CT
L54           4 SEA FILE=MEDLINE ABB=ON  L40 AND L43


L40      277250 SEA FILE=MEDLINE ABB=ON  ISCHEMIA+NT/CT
L41          15 SEA FILE=MEDLINE ABB=ON  TOCOPHEROLS/CT AND DELTA
L55           1 SEA FILE=MEDLINE ABB=ON  L41 AND L40


L40      277250 SEA FILE=MEDLINE ABB=ON  ISCHEMIA+NT/CT
L44         824 SEA FILE=MEDLINE ABB=ON  (BETA OR DELTA OR GAMMA)(A)TOCOPHEROL#

L56       17689 SEA FILE=MEDLINE ABB=ON  FLAVONES+NT/CT
L57           1 SEA FILE=MEDLINE ABB=ON  L40 AND L44 AND L56


L40      277250 SEA FILE=MEDLINE ABB=ON  ISCHEMIA+NT/CT
L44         824 SEA FILE=MEDLINE ABB=ON  (BETA OR DELTA OR GAMMA)(A)TOCOPHEROL#

L56       17689 SEA FILE=MEDLINE ABB=ON  FLAVONES+NT/CT
L60        3264 SEA FILE=MEDLINE ABB=ON  DIOSMIN/CT OR RUTIN+NT/CT OR QUERCETIN
                +NT/CT OR HESPERIDIN/CT
L61        1504 SEA FILE=MEDLINE ABB=ON  CHRYSIN OR DAIDZEIN OR HESPERETIN OR
                LUTEOLIN OR BROMOQUERCETIN OR BIOCHANIN
L69           1 SEA FILE=MEDLINE ABB=ON  L44 AND L40 AND (L56 OR (L60 OR L61))


=> s l54 or l55 or l57 or l69

L110          6 L54 OR L55 OR L57 OR L69

=> fil embase; d que l80

FILE 'EMBASE' ENTERED AT 10:31:46 ON 22 MAY 2003
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 FILE COVERS 1974 TO 19 May 2003 (20030519/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L73      169664 SEA FILE=EMBASE ABB=ON  ISCHEMIA+NT/CT
L74         130 SEA FILE=EMBASE ABB=ON  BETA TOCOPHEROL/CT
L75         498 SEA FILE=EMBASE ABB=ON  GAMMA TOCOPHEROL/CT
L76         128 SEA FILE=EMBASE ABB=ON  DELTA TOCOPHEROL/CT
L80          11 SEA FILE=EMBASE ABB=ON  L73 AND (L74 OR L75 OR L76)


=> fil DRUGU, PASCAL, BIOSIS, WPIDS, SCISEARCH

FILE 'DRUGU' ENTERED AT 10:31:47 ON 22 MAY 2003
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FILE 'PASCAL' ENTERED AT 10:31:47 ON 22 MAY 2003
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FILE 'BIOSIS' ENTERED AT 10:31:47 ON 22 MAY 2003

FILE 'WPIDS' ENTERED AT 10:31:47 ON 22 MAY 2003

FILE 'SCISEARCH' ENTERED AT 10:31:47 ON 22 MAY 2003

=> d que l101;d que l105

L83 5489 SEA (BETA OR GAMMA OR DELTA)(3A) TOCOPHEROL#
L84 403762 SEA ISCHEMI? OR ISCHAEMI? OR ANTIISCHEMI? OR ANTIISCHAEMI?
L96 24736 SEA BETA CAROTENE
L98 39 SEA NON ALPHA TOCOPHEROL#
L100 457 SEA (L83 OR L98)(5A)(TREAT? OR PREVENT? OR ADMIN?)
L101 8 SEA L100 AND L84 NOT L96

L83 5489 SEA (BETA OR GAMMA OR DELTA)(3A) TOCOPHEROL#
L84 403762 SEA ISCHEMI? OR ISCHAEMI? OR ANTIISCHEMI? OR ANTIISCHAEMI?
L96 24736 SEA BETA CAROTENE
L98 39 SEA NON ALPHA TOCOPHEROL#
L99 42 SEA (L83 OR L98) AND L84 NOT L96
L105 21 SEA L99 NOT VITAMIN E

=> s (l101 or l105) not l106

L111 24 (L101 OR L105) NOT L106 printed w/ inventor search

=> dup rem l110,l109,180,l111
FILE 'MEDLINE' ENTERED AT 10:32:11 ON 22 MAY 2003

FILE 'CAPLUS' ENTERED AT 10:32:11 ON 22 MAY 2003

FILE 'EMBASE' ENTERED AT 10:32:11 ON 22 MAY 2003

FILE 'DRUGU' ENTERED AT 10:32:11 ON 22 MAY 2003

FILE 'PASCAL' ENTERED AT 10:32:11 ON 22 MAY 2003

FILE 'BIOSIS' ENTERED AT 10:32:11 ON 22 MAY 2003

FILE 'WPIDS' ENTERED AT 10:32:11 ON 22 MAY 2003

FILE 'SCISEARCH' ENTERED AT 10:32:11 ON 22 MAY 2003

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PROCESSING COMPLETED FOR L110
PROCESSING COMPLETED FOR L109
PROCESSING COMPLETED FOR L80
PROCESSING COMPLETED FOR L111
L112 36 DUP REM L110 L109 L80 L111 (7 DUPLICATES REMOVED)
ANSWERS '1-6' FROM FILE MEDLINE
ANSWERS '7-8' FROM FILE CAPLUS
ANSWERS '9-16' FROM FILE EMBASE
ANSWERS '17-20' FROM FILE DRUGU
ANSWER '21' FROM FILE PASCAL
ANSWERS '22-24' FROM FILE BIOSIS
ANSWERS '25-32' FROM FILE WPIDS
ANSWERS '33-36' FROM FILE SCISEARCH

=> d ibib ab 1-36

L112 ANSWER 1 OF 36 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2002141124 MEDLINE
DOCUMENT NUMBER: 21835493 PubMed ID: 11846411
TITLE: Mixed tocopherol preparation is superior to alpha-tocopherol alone against hypoxia-reoxygenation injury.
AUTHOR: Chen Hongjiang; Li Dayuan; Saldeen Tom; Romeo Francesco; Mehta Jawahar L
CORPORATE SOURCE: Department of Medicine and Physiology, University of Arkansas for Medical Science and Central Arkansas Veterans Health Care System, Little Rock, Arkansas 72205-7199, USA.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2002 Feb 22) 291 (2) 349-53.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020307
Last Updated on STN: 20020320
Entered Medline: 20020319

AB Hypoxia-reoxygenation (H-R) is associated with alterations in oxidant-antioxidant balance and L-arginine-nitric oxide system. Tocopherols decrease the activity of reactive oxygen species (ROS) and yet are not beneficial in clinical trials. It has been proposed that mixed tocopherols as found in nature may be more tissue protective than alpha-tocopherol alone found in commercial preparations. We compared the effect of a mixed tocopherol preparation with that of alpha-tocopherol alone on superoxide dismutase (SOD) activity and iNOS expression in cultured myocytes exposed to H-R. Myocytes from Sprague-Dawley rat hearts were subjected to hypoxia for 24 h followed by reoxygenation for 3 h H-R. Parallel groups of myocytes were pretreated with alpha-tocopherol alone or a mixed-tocopherol preparation (containing alpha-, gamma-, and **delta**-tocopherols) (50 microM) for 30 min. H-R resulted in myocyte injury (determined by LDH release), a decrease in SOD activity and an upregulation of iNOS expression/activity. Both tocopherol preparations attenuated cell injury and markedly decreased the effects of H-R on SOD activity and iNOS expression/activity (all $P < 0.05$ vs H-R group, $n = 5$). However, mixed-tocopherol preparation was much superior to alpha-tocopherol in terms of myocyte protection from the adverse effect of H-R ($P < 0.05$). Lack of efficacy of commercial tocopherol preparations in clinical trials may reflect absence of gamma- and **delta** -tocopherols.

L112 ANSWER 2 OF 36 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2002141572 MEDLINE
DOCUMENT NUMBER: 21870156 PubMed ID: 11880764
TITLE: Dietary and adipose tissue gamma-tocopherol and risk of myocardial infarction.
AUTHOR: El-Sohemy Ahmed; Baylin Ana; Spiegelman Donna; Ascherio Alberto; Campos Hannia
CORPORATE SOURCE: Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts 02115, USA.
CONTRACT NUMBER: HL 49086 (NHLBI)
SOURCE: EPIDEMIOLOGY, (2002 Mar) 13 (2) 216-23.
Journal code: 9009644. ISSN: 1044-3983.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020307
Last Updated on STN: 20020410
Entered Medline: 20020409

AB BACKGROUND: Gamma-tocopherol, the most abundant form of dietary vitamin E, may lower the risk of coronary heart disease. METHODS: We investigated whether dietary and adipose tissue gamma-tocopherol are associated with myocardial infarction (MI) in 475 survivors of a first MI and 479 controls from a population-based study carried out between 1994 and 1998 in Costa Rica. Dietary intake was assessed with a validated food-frequency questionnaire and an adipose tissue sample. Conditional logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CI). RESULTS: Subjects in the highest quintile of dietary gamma-tocopherol had a lower risk of MI compared with those in the lowest quintile (OR = 0.76; 95% CI = 0.50-1.17, P = 0.02 for trend). This trend was no longer statistically substantial in multivariate analysis (P = 0.44). A weak association was found for adipose tissue gamma-tocopherol in univariate (OR = 1.46; 95% CI = 0.94-2.27) and multivariate (OR = 1.31; 95% CI = 0.62-2.76) models. A substantial inverse association with MI was found for total dietary vitamin E whether supplement users were included or excluded (P = 0.01 and 0.05 for trend, respectively). CONCLUSION: These data suggest that gamma-tocopherol does not protect against nonfatal MI.

L112 ANSWER 3 OF 36 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2002120691 MEDLINE
DOCUMENT NUMBER: 21686473 PubMed ID: 11827760
TITLE: Plasma status of retinol, alpha- and gamma-tocopherols, and main carotenoids to first myocardial infarction: case control and follow-up study.
AUTHOR: Ruiz Rejon F; Martin-Pena G; Granado F; Ruiz-Galiana J; Blanco I; Olmedilla B
CORPORATE SOURCE: Servicio de Cardiologia, Servicio de Medicina Interna, Hospital de Mostoles, Madrid, Spain.. ferruiz@inicia.es
SOURCE: NUTRITION, (2002 Jan) 18 (1) 26-31.
Journal code: 8802712. ISSN: 0899-9007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020222
Last Updated on STN: 20020611
Entered Medline: 20020607

AB OBJECTIVE: Epidemiologic studies have suggested that dietary intake and plasma concentrations of antioxidants have an inverse relation with coronary heart disease. To test whether fat-soluble antioxidants can play

a role against the occurrence of myocardial infarction (MI), we measured plasma levels of retinol, tocopherols, and individual carotenoids in MI patients. METHODS: A case-control and follow-up study of patients in the Mostoles area (Madrid, Spain). One hundred six patients (62 after 1 y) and 104 control subjects participated in the study. Blood samples were collected after overnight fast or during the first 24 h of MI onset for biochemical profiles of retinol, alpha- and gamma-tocopherols, and carotenoid by means of a quality-controlled high-performance liquid chromatography. RESULTS: During the acute phase after MI onset, plasma levels of retinol, gamma-tocopherol, and xanthophylls (lutein/zeaxanthin and beta-cryptoxanthin) decreased, whereas alpha-tocopherol, alpha-carotene, beta-carotene, and lycopene showed levels similar to those of control subjects. Logistic regression analysis showed low concentrations of gamma-tocopherol (and retinol) in plasma as the only statistically significant factor associated with MI, after adjusting for traditional risk factors. However, 1 y later, the MI patients showed a general improvement in plasma lipids and fat-soluble antioxidant status, and none of the analytes was associated with MI. CONCLUSIONS: The decreased plasma status of retinol, gamma-tocopherol, and xanthophylls during the acute phase of MI normalized the year after the MI event, suggesting that most subjects had followed an overall healthier lifestyle and dietary pattern. The results also raise concerns on the usefulness of these plasma compounds as specific, relevant, and predictive markers in relation to coronary heart disease.

L112 ANSWER 4 OF 36 MEDLINE
ACCESSION NUMBER: 2002307890 MEDLINE
DOCUMENT NUMBER: 22045028 PubMed ID: 11960550
TITLE: Evidence for the nitration of gamma-tocopherol in vivo: 5-nitro-gamma-tocopherol is elevated in the plasma of subjects with coronary heart disease.
AUTHOR: Morton Lincoln W; Ward Natalie C; Croft Kevin D; Puddey Ian B
CORPORATE SOURCE: Department of Medicine, University of Western Australia and Western Australian Institute for Medical Research, PO Box X2213, GPO Perth, Western Australia, 6001, Australia.
SOURCE: BIOCHEMICAL JOURNAL, (2002 Jun 15) 364 (Pt 3) 625-8. Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020611
Last Updated on STN: 20020816
Entered Medline: 20020815

AB This study investigated the hypothesis that nitration of gamma-tocopherol may be an important mechanism for the detoxification of reactive nitrogen oxide species in vivo. Using liquid chromatography-tandem MS we have shown that gamma-tocopherol can be nitrated in vivo to form 5-nitro-gamma-tocopherol and that concentrations of this compound are elevated in the plasma of subjects with coronary heart disease. In addition, we demonstrate in carotid-artery atherosclerotic plaque that nitration of gamma-tocopherol is also evident at levels similar to that seen in the plasma of subjects with coronary heart disease.

L112 ANSWER 5 OF 36 MEDLINE
ACCESSION NUMBER: 2002201460 MEDLINE
DOCUMENT NUMBER: 21930918 PubMed ID: 11933918
TITLE: Association of serum antioxidant capacity with coronary artery disease in middle-aged men.
AUTHOR: Nojiri S; Daida H; Mokuno H; Iwama Y; Mae K; Ushio F; Ueki T

CORPORATE SOURCE: Tama Branch, Tokyo Metropolitan Research Laboratory of Public Health, Japan.
SOURCE: JAPANESE HEART JOURNAL, (2001 Nov) 42 (6) 677-90. Journal code: 0401175. ISSN: 0021-4868.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020406
Last Updated on STN: 20020412
Entered Medline: 20020410

AB The possible involvement of oxidative damage in the progression of atherosclerosis has been suggested. There is some evidence that antioxidant therapy may be beneficial for the prevention of coronary heart disease. In this study, we investigated the relationship between coronary artery disease (CAD) and serum antioxidative status by measuring the total antioxidant status (TAS). Other relevant antioxidants, such as retinol, alpha, gamma-tocopherol, ascorbic acid, alpha, beta-carotenoids, erythrocyte glutathione peroxidase (GSH-Px) and oxidative products, were also determined in 31 male CAD patients with angiographically defined CAD and 66 male controls, aged 40-70 years, in a case-control study. The TAS levels, ratio and the concentrations of retinol, albumin, total protein and HDL cholesterol were significantly lower in the CAD patients than in the controls ($p<0.01$), and alpha-tocopherol and alpha/gamma-tocopherol were significantly higher in the CAD patients than in the controls. The TAS level correlated positively with gamma-GTP, GPT, GOT and uric acid ($p<0.01$). A multiple regression analysis in the CAD patients revealed that the TAS levels correlated most negatively with the number of diseased vessels. The concentrations of carotenoids and GSH-Px, as well as the alpha/gamma-tocopherol ratio were also significantly associated. Although conditional logistic regression analysis suggested low levels of HDL-cholesterol to be a significant coronary risk factor (OR=5.1, 95% CI=1.09-24.3), the TAS level showed no significant independent contribution to CAD. This study demonstrated an association of antioxidant parameters with the atherosclerosis progression, however, it did not confirm antioxidants as an independent risk factor for CAD event.

L112 ANSWER 6 OF 36 MEDLINE
ACCESSION NUMBER: 2001115601 MEDLINE
DOCUMENT NUMBER: 21019758 PubMed ID: 11138821
TITLE: Intake of flavonols and flavones and risk of coronary heart disease in male smokers.
AUTHOR: Hirvonen T; Pietinen P; Virtanen M; Ovaskainen M L; Hakkinen S; Albanes D; Virtamo J
CORPORATE SOURCE: Department of Nutrition, National Public Health Institute, Helsinki, Finland.
CONTRACT NUMBER: NO1-CN-45165 (NCI)
SOURCE: EPIDEMIOLOGY, (2001 Jan) 12 (1) 62-7. Journal code: 9009644. ISSN: 1044-3983.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010215

AB Flavonols and flavones are antioxidant polyphenolic compounds found in tea, vegetables, fruits, and wine. In experimental studies they have been effective free radical scavengers, metal chelators, and antithrombotic

agents. In the few epidemiologic studies of these agents, some have suggested an inverse association between intake of flavonols and flavones and the risk of cardiovascular disease. Our study population comprised 25,372 male smokers, 50-69 years of age, with no previous myocardial infarction. They were participants of the Alpha-**Tocopherol**, **Beta**-Carotene Cancer Prevention Study, which was a randomized, double-blind, placebo-controlled trial with daily supplementation of alpha-tocopherol (50 mg per day) and/or beta-carotene (20 mg per day). The men completed a validated dietary questionnaire at baseline. After 6.1 years of follow-up, there were 1,122 nonfatal myocardial infarctions and 815 coronary deaths. In the multivariate model, the relative risk of nonfatal myocardial infarction was 0.77 (95% confidence interval = 0.64-0.93) among men in the highest (median 18 mg per day) compared with the lowest (median 4 mg per day) quintile of flavonol and flavone intake. The respective relative risk for coronary death was 0.89 (95% confidence interval = 0.71-1.11). Thus, intake of flavonols and flavones was inversely associated with nonfatal myocardial infarction, whereas there was a weaker association with coronary death.

L112 ANSWER 7 OF 36 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 5
ACCESSION NUMBER: 2000:238052 CAPLUS
DOCUMENT NUMBER: 132:260686
TITLE: Use of .**gamma**.-**tocopherol** and its oxidative metabolite LLU-.alpha. in the treatment of natriuretic disease
INVENTOR(S): Wechter, William J.
PATENT ASSIGNEE(S): Loma Linda University Medical Center, USA
SOURCE: U.S., 21 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6048891	A	20000411	US 1998-215608	19981217
US 6242479	B1	20010605	US 1999-461645	19991214
WO 2000035444	A1	20000622	WO 1999-US30100	19991216
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1140065	A1	20011010	EP 1999-968905	19991216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002532421	T2	20021002	JP 2000-587764	19991216
US 2001031782	A1	20011018	US 2001-814330	20010321
US 6410589	B2	20020625		
US 2002165268	A1	20021107	US 2002-134140	20020426
US 6555575	B2	20030429		

PRIORITY APPLN. INFO.: US 1998-215608 A1 19981217
US 1999-461645 A1 19991214
WO 1999-US30100 W 19991216
US 2001-814330 A1 20010321
OTHER SOURCE(S): MARPAT 132:260686
AB The invention is generally related to the discovery of the therapeutic benefit of administering .gamma.-tocopherol and .gamma.-tocopherol derivs. More specifically, the use of .gamma.-tocopherol and racemic LLU-.alpha., (S)-LLU-.alpha., or .gamma.-tocopherol derivs. as antioxidants and nitrogen oxide scavengers which treat and prevent high blood pressure, thromboembolic disease, cardiovascular disease, cancer, natriuretic disease, the formation of neuropathol. lesions, and a reduced immune system response are disclosed.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L112 ANSWER 8 OF 36 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:169475 CAPLUS
DOCUMENT NUMBER: 128:248580
TITLE: Association of NO synthase inhibitors with trappers of reactive oxygen species
INVENTOR(S): Chabrier De Lassauniere, Pierre-Etienne; Bigg, Denis
PATENT ASSIGNEE(S): Societe De Conseils De Recherches Et D'applications Scientifiques (S.C.R.A.S, Fr.; Chabrier De Lassauniere, Pierre-Etienne; Bigg, Denis
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809653	A1	19980312	WO 1997-FR1567	19970905
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2753098	A1	19980313	FR 1996-10875	19960906
FR 2753098	B1	19981127		
AU 9742111	A1	19980326	AU 1997-42111	19970905
AU 734296	B2	20010607		
EP 939654	A1	19990908	EP 1997-940183	19970905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 334597	A	20001027	NZ 1997-334597	19970905
JP 2000517336	T2	20001226	JP 1998-512314	19970905
RU 2174844	C2	20011020	RU 1999-106792	19970905
US 6297281	B1	20011002	US 1999-254254	19990302
NO 9901100	A	19990505	NO 1999-1100	19990305

PRIORITY APPLN. INFO.: FR 1996-10875 A 19960906
WO 1997-FR1567 W 19970905

AB The invention concerns a pharmaceutical compn. contg., as active principle, at least one NO synthase-inhibiting substance and at least one reactive oxygen-trapping substance, optionally with a pharmaceutically acceptable support. The invention also concerns a product contg. at least one NO synthase-inhibiting substance and at least one reactive oxygen-trapping substance as combined product of these active principles in sep. form.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L112 ANSWER 9 OF 36 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 1
ACCESSION NUMBER: 2003030610 EMBASE
TITLE: Vitamin E isoforms .alpha.-tocotrienol and .gamma.-tocopherol prevent cerebral infarction in mice.
AUTHOR: Mishima K.; Tanaka T.; Pu F.; Egashira N.; Iwasaki K.; Hidaka R.; Matsunaga K.; Takata J.; Karube Y.; Fujiwara M.
CORPORATE SOURCE: M. Fujiwara, Department of Neuropharmacology, Faculty of Pharmaceutical Sciences, Fukuoka University, Fukuoka 814-0180, Japan. mfuji@fukuoka-u.ac.jp

SOURCE: Neuroscience Letters, (30 Jan 2003) 337/1 (56-60).
Refs: 23
ISSN: 0304-3940 CODEN: NELED5
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB .alpha.-tocopherol and its derivatives have been shown to be effective in reducing cerebral ischemia-induced brain damage. However, the effects of other vitamin E isoforms have not been characterized. In the present study, we investigated the effects of six different isoforms of vitamin E on the ischemic brain damage in the mice middle cerebral artery (MCA) occlusion model. All vitamin E isoforms were injected i.v., twice, immediately before and 3 h after the occlusion. .alpha.-tocopherol (2 mM), .alpha.-tocotrienol (0.2 and 2 mM) and .gamma.-tocopherol (0.2 and 2 mM) significantly decreased the size of the cerebral infarcts 1 day after the MCA occlusion, while .gamma.-tocotrienol, .delta.-tocopherol and .delta.-tocotrienol showed no effect on the cerebral infarcts. These results suggest that .alpha.-tocotrienol and .gamma.-tocopherol are potent and effective agents for preventing cerebral infarction induced by MCA occlusion. .COPYRGT. 2002 Elsevier Science Ireland Ltd. All rights reserved.

L112 ANSWER 10 OF 36 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002377361 EMBASE
TITLE: Prevention of restenosis with antioxidants: Mechanisms and implications.
AUTHOR: Tardif J.-C.; Gregoire J.; L'Allier P.L.
CORPORATE SOURCE: Dr. J.-C. Tardiff, Montreal Heart Institute, 5000 Belanger Street, Montreal, Que. H1T 1C8, Canada.
tardifjc@icm.umontreal.ca
SOURCE: American Journal of Cardiovascular Drugs, (2002) 2/5 (323-334).
Refs: 103
ISSN: 1175-3277 CODEN: AJCDDJ
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The aim of this review is to give an overview of the field of restenosis prevention with antioxidants, put in perspective of their potential use for the prevention of atherosclerosis progression. Compelling evidence points to oxidative stress as an important trigger in the complex chain of events leading to atherosclerosis. There is also evidence that oxidative stress occurs early after angioplasty. Reactive oxygen species (ROS) can induce endothelial dysfunction and macrophage activation, resulting in the release of cytokines and growth factors that stimulate matrix remodeling and smooth muscle cell proliferation. The accumulation of new extracellular matrix and smooth muscle cells will result in the neointimal formation responsible for lumen narrowing after stent deployment and which contributes to that after balloon angioplasty. In addition, oxidation processes are involved in the cross-linking of collagen fibers, and this coupled with smooth muscle cell contraction and endothelial dysfunction may result in long-term vascular constriction or lack of adaptive vascular remodeling after balloon angioplasty. The powerful antioxidant probucol

has been shown to prevent coronary restenosis after balloon angioplasty in the Multivitamins and Probucol (MVP) trial and other clinical studies. However, prolongation of the QT interval with probucol remains a long-term safety concern. AGI-1067, a metabolically stable analog of probucol, is a vascular protectant with strong antioxidant properties as potent to those of probucol. There has been no evidence of prolongation of the QT interval with AGI 1067 in initial clinical studies. The anti-restenosis properties of AGI-1067 are being assessed in the Canadian Antioxidant Restenosis Trial (CART)-1. Considering that oxidative stress and inflammation may persist for a prolonged period after stent placement, treatment with AGI-1067 for the entire period of risk after percutaneous coronary intervention (PCI) [instead of only 4 weeks in CART- 1] may result in enhanced protection against luminal renarrowing. This hypothesis will be tested in the randomized, multicenter CART-2 trial. AGI-1067 has been effective at preventing atherosclerosis in all tested animal models, including the low density lipoprotein receptor-deficient and apo-E knockout mice. This has potentially important implications, as PCI and local approaches to prevent restenosis such as coated stents are not expected to prevent atherosclerosis progression, myocardial infarction and cardiovascular death. As the ultimate goal of therapy for patients with coronary artery disease must remain prevention of disease progression and atherosclerosis-related events, CART-2 will test the value of AGI-1067 for the reduction of both post-PCI restenosis and atherosclerosis progression.

L112 ANSWER 11 OF 36 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002170028 EMBASE
TITLE: Melatonin and the cardiovascular system.
AUTHOR: Sewerynek E.
CORPORATE SOURCE: Dr. E. Sewerynek, Department of Thyroidology, Institute of Endocrinology, Medical University of Lodz, Sterlinga Str 5, 91-425 Lodz, Poland. ewa@tyreo.am.lodz.pl
SOURCE: Neuroendocrinology Letters, (2002) 23/SUPPL. 1 (79-83).
Refs: 66
ISSN: 0172-780X CODEN: NLETDU
COUNTRY: Sweden
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Melatonin concentrations in serum, as well as urinary levels of its main metabolite, 6-sulphatoxy-melatonin, decrease with age. In the course of aging, the frequency of heart diseases, both acute and chronic, systematically increases. The evidence from the last 10 years suggests that melatonin influences the cardiovascular system. The presence of vascular melatoninergic receptors/binding sites has been demonstrated; these receptors are functionally linked with vasoconstrictor or vasodilatory effects of melatonin. Melatonin can contribute in cardioprotection of the rat heart, following myocardial ischemia. It has been shown that patients with coronary heart disease have a low melatonin production rate, especially those with higher risk of cardiac infarction and/or sudden death. There are clinical data reporting some alterations of melatonin in human stroke and coronary heart disease. The suprachiasmatic nucleus and, possibly, the melatoninergic system may also modulate cardiovascular rhythmicity. Hypercholesterolemia and hypertension are the other age-related symptoms. People with high levels of LDL-cholesterol have low levels of melatonin. It has been shown that melatonin suppresses the formation of cholesterol by 38% and reduces LDL accumulation by 42%. A 10-20% reduction of cholesterol concentration in women using the B-oval pill has been observed. It is a very important because, even a 10-15% reduction in blood cholesterol concentration has bee shown to result in a

20 to 30% decrease in the risk of coronary heart disease. People with hypertension have lower melatonin levels than those with normal blood pressure. The administration of the hormone in question declines blood pressure to normal range. It has been observed that melatonin, even in a dose 1 mg, reduced blood pressure and decreased catecholamine level after 90 min in human subjects. Melatonin may reduce blood pressure via the following mechanisms: 1) by a direct effect on the hypothalamus; 2) as an antioxidant which lowers blood pressure; 3) by decreasing the level of catecholamines, or 4) by relaxing the smooth muscle in the aorta wall.

L112 ANSWER 12 OF 36 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002020855 EMBASE
TITLE: What's hot in the prostate?.
AUTHOR: Belldegrun A.
CORPORATE SOURCE: A. Belldegrun, Department of Urology, UCLA School of Medicine, Los Angeles, CA, United States
SOURCE: Prostate Cancer and Prostatic Diseases, (2001) 4/4 (191-194).
ISSN: 1365-7852 CODEN: PCPDFW
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 016 Cancer
028 Urology and Nephrology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L112 ANSWER 13 OF 36 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999226780 EMBASE
TITLE: Vitamin E: Function and metabolism.
AUTHOR: Brigelius-Flohe R.; Traber M.G.
CORPORATE SOURCE: R. Brigelius-Flohe, German Institute of Human Nutrition, Arthur Scheunert-Allee 114-116, D-14558 Bergholz-Rehbrucke, Germany
SOURCE: FASEB Journal, (1999) 13/10 (1145-1155).
Refs: 112
ISSN: 0892-6638 CODEN: FAJOEC
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
028 Urology and Nephrology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Although vitamin E has been known as an essential nutrient for reproduction since 1922, we are far from understanding the mechanisms of its physiological functions. Vitamin E is the term for a group of tocopherols and tocotrienols, of which .alpha.-tocopherol has the highest biological activity. Due to the potent antioxidant properties of tocopherols, the impact of .alpha.- tocopherol in the prevention of chronic diseases believed to be associated with oxidative stress has often been studied, and beneficial effects have been demonstrated. Recent observations that the .alpha.-tocopherol transfer protein in the liver specifically sorts out RRR-.alpha.-tocopherol from all incoming tocopherols for incorporation into plasma lipoproteins, and that .alpha.-tocopherol has signaling functions in vascular smooth muscle cells that cannot be exerted by other forms of tocopherol with similar antioxidative properties, have raised interest in the roles of vitamin E beyond its antioxidative function. Also, .gamma.-tocopherol might have functions apart from being an antioxidant. It is a nucleophile able to trap electrophilic mutagens in lipophilic compartments and generates a

metabolite that facilitates natriuresis. The metabolism of vitamin E is equally unclear. Excess .alpha.- tocopherol is converted into .alpha.-CEHC and excreted in the urine. Other tocopherols, like .gamma.- and .delta.-tocopherol, are almost quantitatively degraded and excreted in the urine as the corresponding CEHCs. All rac .alpha.-tocopherol compared to RRR-.alpha.-tocopherol is preferentially degraded to .alpha.-CEHC. Thus, there must be a specific, molecular role of RRR-.alpha.-tocopherol that is regulated by a system that sorts, distributes, and degrades the different forms of vitamin E, but has not yet been identified. In this article we try to summarize current knowledge on the function of vitamin E, with emphasis on its antioxidant vs. other properties, the preference of the organism for RRR.alpha.-tocopherol, and its metabolism to CEHCs.

L112 ANSWER 14 OF 36 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999012391 EMBASE
TITLE: Consumption of vitamin E in coronary circulation in patients with variant angina.
AUTHOR: Miwa K.; Igawa A.; Nakagawa K.; Hirai T.; Inoue H.
CORPORATE SOURCE: K. Miwa, Department of Internal Medicine, Toyama Med. and Pharmaceut. Univ., 2630 Sugitani, Toyama 930-0194, Japan. kmiwa@ms.toyama-mpu.ac.jp
SOURCE: Cardiovascular Research, (1999) 41/1 (291-298).
Refs: 30
ISSN: 0008-6363 CODEN: CVREAU
PUBLISHER IDENT.: S 0008-6363(98)00207-7
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objectives: The plasma status of vitamin E has been suggested to be linked to the activity of coronary artery spasm. This study was designed to determine whether vitamin E is actually consumed in the coronary circulation in patients with active variant angina having repetitive spasm-induced transient myocardial ischemia and reperfusion. Methods: Blood samples were obtained simultaneously from the aortic root, coronary sinus and right atrium in 12 patients with variant angina due to spasm of the left coronary artery, nine patients with stable effort angina and nine control subjects. Plasma vitamin E (.alpha.- and .gamma.-tocopherol) concentrations were determined by use of high-performance liquid chromatography and plasma lipid peroxides were measured as thiobarbituric acid-reactive substances (TBARS). Results: At baseline, both plasma .alpha.- ($p<0.01$) and .gamma.- ($p<0.05$) tocopherol levels were significantly lower in the coronary sinus (5.50.+-.0.50 and 0.55.+-.0.07 mg/l, mean.+-.SEM) than in the aortic root (6.63.+-.0.57 and 0.63.+-.0.08 mg/l) and also in the right atrium (6.44.+-.0.61 and 0.63.+-.0.09 mg/l) in the variant angina group. The TBARS level was significantly ($p<0.05$) higher in the coronary sinus than in the aortic root in this group. In contrast, these levels were not significantly different between the samples from the coronary sinus and the aortic root or the right atrium in the control group and also in the stable effort angina group. The coronary sinus-aortic difference in plasma vitamin E levels in the variant angina group was not significantly altered after left coronary artery spasm induced by intracoronary injection of acetylcholine. Also, the plasma vitamin E levels in the aortic root, coronary, sinus and right atrium all remained unchanged in the stable effort angina group after pacing-induced angina and in the control group after intracoronary administration of acetylcholine. Conclusions: Transcardiac reduction in plasma vitamin E concentrations concomitant with lipid peroxide formation was demonstrated in patients with active variant angina, suggesting actual consumption of this major endogenous antioxidant. Oxidative stress and vitamin E exhaustion may be involved in the pathogenesis of coronary artery spasm.

L112 ANSWER 15 OF 36 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998041587 EMBASE
TITLE: Prospective association between lipid soluble antioxidants and coronary heart disease in men. The multiple risk factor intervention trial.
AUTHOR: Evans R.W.; Shaten B.J.; Day B.W.; Kuller L.H.
CORPORATE SOURCE: Dr. R.W. Evans, University of Pittsburgh, Graduate School of Public Health, Parran Hall, 130 DeSoto Street, Pittsburgh, PA 15261, United States
SOURCE: American Journal of Epidemiology, (15 Jan 1998) 147/2 (180-186).
Refs: 44
ISSN: 0002-9262 CODEN: AJEPAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A nested case-control study was performed using participants enrolled in the Multiple Risk Factor Intervention Trial (MRFIT). The cases involved nonfatal myocardial infarction or death from coronary heart disease. Serum samples (n = 734) obtained at baseline and frozen for approximately 20 years were analyzed for the antioxidants, carotenoids, retinol, and .alpha.-, .gamma.-, and total tocopherol. The concentrations of antioxidants were in the expected range and their association with low density lipoprotein (LDL) cholesterol reflected their absorption and transport mechanisms. Among nonsmokers, the odds ratios (95% confidence intervals (CI)) for quartile IV versus quartile I were 1.40 (0.40-4.89), 0.77 (0.20-2.96), 1.45 (0.38-5.56), 2.34 (0.56-9.81), and 2.40 (0.52-11.07) for retinol, total carotenoids, and .alpha.-, .gamma.-, and total tocopherol, respectively. The equivalent odds ratios (95% CI) for smokers were 0.90 (0.34-2.41), 0.66 (0.23-1.84), 0.67 (0.21-2.13), 2.04 (0.88-4.73), and 0.52 (0.16-1.67), respectively. This analysis of antioxidant concentrations by quartiles indicated no significant association of antioxidant levels with the risk of coronary disease death or nonfatal myocerdial infarction.

L112 ANSWER 16 OF 36 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96304142 EMBASE
DOCUMENT NUMBER: 1996304142
TITLE: Predictors of adipose tissue tocopherol and toenail selenium levels in nine countries: The EURAMIC study.
AUTHOR: Virtanen S.M.; Van't Veer P.; Kok F.; Kardinaal A.F.M.
CORPORATE SOURCE: Tampere School of Public Health, University of Tampere, PO Box 607,FIN-33101 Tampere, Finland
SOURCE: European Journal of Clinical Nutrition, (1996) 50/9 (599-606).
ISSN: 0954-3007 CODEN: EJCNEQ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Objective: To evaluate the levels of adipose tissue alpha-tocopherol, gamma-tocopherol, and toenail selenium and their determinants. Design: Control subjects from multicentre case-control study on antioxidants, myocardial infarction and cancer of the breast. Subjects and setting: 686 male and 339 female middle-aged and elderly subjects from eight European countries and Israel. Results: The antioxidant levels were lower in men than women; adipose tissue alpha-tocopherol level in men was 75% of that in women, gamma-tocopherol 79%, and toenail selenium 92%, respectively. In

multiple regression analysis adjusting for age and centre waist circumference showed to be the only independent predictor of adipose tissue alpha-tocopherol level and waist/hip (W/H) ratio that of gamma-tocopherol level in men. In women no predictors of adipose tissue alpha-tocopherol or gamma-tocopherol level were found. Smoking and coffee use showed up to be the independent predictors of toenail selenium in men and smoking in women. Age, alcohol use, serum lipids, and reproductive factors were not related to the antioxidant levels. Conclusion: The inverse relationships of adipose tissue alpha-tocopherol and gamma-tocopherol levels with central fat distribution should be considered in studies relating the tocopherol levels to the development of chronic diseases in men, and the inverse relationship of toenail selenium with smoking both in men and women, and with coffee consumption in men, should be considered when toenail selenium level is used as a biomarker in epidemiological studies.

L112 ANSWER 17 OF 36 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 1998-14229 DRUGU T
TITLE: Gemfibrozil-induced decrease in serum ubiquinone and alpha- and **gamma-tocopherol** levels in men with combined hyperlipidaemia.
AUTHOR: Aberg F; Appelkvist E L; Broijersen A; Eriksson M; Angelin B; Hjemdah P
CORPORATE SOURCE: Karolinska-Inst.
LOCATION: Novum, Karolinska; Huddinge, Swed.
SOURCE: Eur.J.Clin.Invest. (28, No. 3, 235-42, 1998) 3 Fig. 3 Tab. 46 Ref.
CODEN: EJCIB8 ISSN: 0014-2972
AVAIL. OF DOC.: Clinical Research Center, Novum, S-141 86 Huddinge, Sweden. (E.L.A.). (E-mail: Eeva-Liisa.Appelkvist@kfc.hs.sll.se).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The influence of p.o. gemfibrozil therapy (Lopid, Parke-Davis) on the serum concentration of antioxidant lipids, was assessed in 21 patients with combined hyperlipidemia in a randomized, double-blind, placebo-controlled, cross-over study. Gemfibrozil lowered the levels of serum cholesterol, triglycerides and antioxidants in these patients. Concomitant therapy included diuretics, beta blockers, ACE inhibitors, allopurinol, calcium antagonists and clomipramine. The mechanism of the effects of gemfibrozil needs further investigation.

L112 ANSWER 18 OF 36 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 1995-29328 DRUGU T
TITLE: Acute cerebral infarction. Optimal management in older patients.
AUTHOR: Langhorne P; Stott D J
LOCATION: Glasgow, U.k.
SOURCE: Drugs Aging (6, No. 6, 445-55, 1995) 6 Tab. 46 Ref. ISSN: 1170-229X
AVAIL. OF DOC.: Academic Section of Geriatric Medicine, Royal infirmary, Glasgow G4 0SF, Scotland.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Optimal management of acute cerebral infarction in the older patient is reviewed with reference to diagnosis (stroke or non-stroke, infarction or hemorrhage), causal factors, symptomatology, general care, acute treatment (improving cerebral perfusion, neuroprotection of **ischemic** neurones, agents which reduce cerebral edema) and subsequent prevention of recurrent episodes (managing the underlying

cause, management of risk factors (B.P., cholesterol), antithrombotic therapies (prevention of vascular events and of venous thromboembolism) and carotid surgery/angioplasty).

L112 ANSWER 19 OF 36 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 1993-29390 DRUGU T P
TITLE: Phosphocreatine: Molecular and Cellular Aspects of the Mechanism of Cardioprotective Action.
AUTHOR: Saks V A; Strumia E
CORPORATE SOURCE: Schiaparelli-Searle
LOCATION: Moscow, Russia, Torino, Italy
SOURCE: Curr.Ther.Res. (53, No. 5, 565-98, 1993) 23 Fig. 102 Ref.
CODEN: CTCEA9 ISSN: 0011-393X
AVAIL. OF DOC.: Schiapparelli Searle, Corso Belgio n. 86, 10153 Torino, Italy.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Phosphocreatine (PCr, Neoton, Schiapparelli-Searle) is reviewed for its cardioprotective action. In MI, PCr is antiarrhythmic, improves diastolic function and reduces heart failure. In cardiac surgery, PCr in cardioplegic solutions improves function and reduces post operative inotropic support. The mechanisms involved include protection against lipid peroxidation and the action of H2O2, inhibition of membrane phospholipid metabolism and of lysophosphoglyceride accumulation, increase of the heart nucleotide pool, a direct action on membrane structure, a zwitterionic action on the sarcolemma, prevention of immunocytotoxic injury and beneficial effects on RBC. Comparisons with phosphoarginine, **tocopherol** phosphate (TPP) and **beta** -blockers are drawn.

L112 ANSWER 20 OF 36 DRUGU COPYRIGHT 2003 THOMSON DERWENT
ACCESSION NUMBER: 1986-17853 DRUGU T S E
TITLE: Open-Labeled Phase III Clinical Trials with Vinpocetine in Japan.
AUTHOR: Ebi O
CORPORATE SOURCE: Takeda
LOCATION: Osaka, Japan
SOURCE: Ther.Hung. (33, No. 1, 41-49, 1985) 5 Tab. 22 Ref.
CODEN: THHUAF ISSN: 0133-3909
AVAIL. OF DOC.: Development Department New Product Planning & Developement Division, Takeda Chemical Industries, Ltd., Osaka, Japan.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Treatment with p.o. TCV-3B (vinpocetine) improved subjective symptoms, disturbances in daily life activity (DLA), and psychic and neurologic symptoms in open-labeled phase III trials among 288 patients with cerebrovascular disorders. Side effects were nausea, upper abdominal pain, diarrhea (treated with lactobacillus), stomatitis, eruption (treated with chlorpheniramine maleate, betamethasone, diphenhydramine and Ca bromide), urticaria, dizziness, flushing, and epileptiform convulsions (treated with phenytoin, phenobarbital and carbamazepine).Concomitant drugs included Na dextran sulfate, mefenamate, vitamins B1, B6 and B12, tolperisone, ketoprofen, hydralazine, dipyridamole, methyldopa, propranolol, oryzanol-**gamma**, trichlormethiazide, **tocopherol** acetate, and penflutizide.

L112 ANSWER 21 OF 36 PASCAL COPYRIGHT 2003 INIST-CNRS. ALL RIGHTS RESERVED.
ACCESSION NUMBER: 2003-0061742 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2003 INIST-CNRS. All rights

reserved.
TITLE (IN ENGLISH): .alpha.-Tocopherol prevents apoptosis of vascular endothelial cells via a mechanism exceeding that of mere antioxidation
AUTHOR: UEMURA Manabu; MANABE Hiroki; YOSHIDA Norimasa; FUJITA Noriko; OCHIAI Jun; MATSUMOTO Naohisa; TAKAGI Tomohisa; NAITO Yuji; YOSHIKAWA Toshikazu
CORPORATE SOURCE: First Department of Internal Medicine, Kyoto Prefectural University of Medicine, 465, Kajii-cho, Kawaramachi, Hirokouji, Kamigyo, Kyoto 602-0841, Japan
SOURCE: European journal of pharmacology, (2002), 456(1-3), 29-37, refs. 1 p.1/4
ISSN: 0014-2999 CODEN: EJPHAZ
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Netherlands
LANGUAGE: English
AVAILABILITY: INIST-13322, 354000106794140040
AB .alpha.-Tocopherol has been reported to exert an anti-atherogenesis effect. We attempted to clarify the effect of .alpha.-tocopherol-both as an antioxidant and as a nonantioxidant-on apoptosis induced by oxidized low-density lipoprotein (LDL) or oxysterols. Oxidized LDL and oxysterols induced necrosis and/or apoptosis of vascular endothelial cells. The induction of apoptosis was associated with increased caspase-3 activity and the generation of intracellular reactive oxygen species, both the effects of which were attenuated by .alpha.-tocopherol. Apoptosis was also decreased by **.beta.-tocopherol** or intracellular radical scavengers, but these suppressive effects were less than those of .alpha.-**tocopherol**. Neither **.beta.-tocopherol** nor the scavengers had pronounced effect on caspase-3 activity, but each of them decreased the generation of reactive oxygen species to the same extent as .alpha.-tocopherol. Our study suggests that .alpha.-Toc protects against apoptosis not only by scavenging reactive oxygen species, but also by inhibiting caspase activity, which means that its activity may exceed that of a mere antioxidant.

L112 ANSWER 22 OF 36 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6
ACCESSION NUMBER: 1997:15090 BIOSIS
DOCUMENT NUMBER: PREV199799314293
TITLE: Lipid peroxidation-associated oxidative stress during percutaneous transluminal coronary angioplasty in humans.
AUTHOR(S): Oostenburg, Gerard S. (1); Mensink, Ronald P.; Bar, Frits W. H. M.; Hornstra, Gerard
CORPORATE SOURCE: (1) Dep. Human Biol., Maastricht Univ., PO Box 616, 6200 Maastricht Netherlands
SOURCE: Free Radical Biology & Medicine, (1997) Vol. 22, No. 1-2, pp. 129-136.
ISSN: 0891-5849.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Animal studies suggest that myocardial **ischemia**/reperfusion causes oxidative stress. We, therefore, examined whether routinely performed percutaneous transluminal coronary angioplasty (PTCA) might be a human **ischemia**/reperfusion model for oxidative stress-induced lipid peroxidation. Fasting antecubital venous blood was sampled from 13 patients on the morning of PTCA, and 2 d after PTCA. Venous and coronary arterial blood were sampled just before and 10 min after the first balloon inflation. Samples were analyzed for plasma and LDL lipid hydroperoxide levels, in vitro oxidation of LDL, and LDL antioxidant levels. Lipid hydroperoxide levels in plasma and LDL remained unchanged throughout the study. During the first 10 min of PTCA, the lag time during oxidation of LDL in vitro did not change, but the maximum rate of oxidation decreased

in venous and arterial samples (Wilcoxon signed rank test: p lt .002). At the same time, total tocopherol levels in LDL significantly increased by 6.3% (p = .048) in arterial, but not in venous samples. Total carotenoid levels increased by 3.8% (p = .127) in arterial samples and decreased by 2.9% (p = .040) in venous samples. Forty hours after PTCA, LDL oxidation parameters and LDL antioxidant levels were similar to baseline, except for about 17% lower levels of **delta-tocopherol** (p = .037) and **gamma-tocopherol** (p = .014). Our results, therefore, do not support that PTCA in humans is associated with oxidative stress-induced lipid peroxidation.

L112 ANSWER 23 OF 36 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:194953 BIOSIS
DOCUMENT NUMBER: PREV200200194953
TITLE: Desmethyl tocopherols for protecting cardiovascular tissue.
AUTHOR(S): Hensley, Kenneth L. (1); Floyd, Robert A.
CORPORATE SOURCE: (1) Oklahoma City, OK USA
ASSIGNEE: Oklahoma Medical Research Foundation
PATENT INFORMATION: US 6346544 February 12, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 12, 2002) Vol. 1255, No. 2, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
AB The present invention involves the use of desmethyl **tocopherols** such as **gamma tocopherol** for the protection of cardiovascular tissue from nitrative stress. While mechanisms other than scavenging of reactive nitrogen species may be involved, desmethyl tocopherols exhibit significant protection and may be utilized to treat or help prevent cardiovascular particularly arterial vascular disease. The desmethyl tocopherols may be administered dietarily or parenterally when a more direct dosage is desired. Both routes may be utilized together or separately to optimize therapeutic and prophylactic benefits. The lessening of damage induced by reactive nitrogen species leads to the lessening of arterial blockage in thrombosis.

L112 ANSWER 24 OF 36 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:104554 BIOSIS
DOCUMENT NUMBER: PREV200100104554
TITLE: Oral consumption of purple grape juice increases plasma antioxidant levels and antioxidant capacity.
AUTHOR(S): Freedman, Jane E. (1); Iafrati, Mark D.; Deak, Leslie R.; Ivanov, Vadim; Folts, John D.; Frei, Balz
CORPORATE SOURCE: (1) Georgetown Univ Medical Ctr, Washington, DC USA
SOURCE: Circulation, (October 31, 2000) Vol. 102, No. 18 Supplement, pp. II.82-II.83. print.
Meeting Info.: Abstracts from Scientific Sessions 2000 New Orleans, Louisiana, USA November 12-15, 2000
ISSN: 0009-7322.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L112 ANSWER 25 OF 36 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-454621 [48] WPIDS
DOC. NO. CPI: C2002-129286
TITLE: Composition useful as scavenger of free radicals comprises a combination of delta-tocol with polyphenols.
DERWENT CLASS: B05 D13 D21 E13 E14
INVENTOR(S): HASLER-NGUYEN, N; TROUP, J P; ZIJLSTRA, J
PATENT ASSIGNEE(S): (NOVS) NOVARTIS NUTRITION AG

COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002034072	A2	20020502	(200248)*	EN	27
AU 2002019051	A	20020506	(200257)		

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002034072	A2	WO 2001-EP12188	20011022
AU 2002019051	A	AU 2002-19051	20011022

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002019051	A	Based on	WO 200234072

PRIORITY APPLN. INFO: GB 2000-26018 20001024

AB WO 200234072 A UPAB: 20020730
NOVELTY - A composition (I) comprises a mixture of a source of delta -tocol (a) comprising greater than 2 wt.% delta -tocol and polyphenols (b). When (b) is citrus flavanoid, (a) is **delta - tocopherol.**

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the followings:

(1) A nutritional product comprising (I);

(2) A food or beverage product comprising (a), an antioxidant source comprising (b), and optionally at least one of carbohydrate, fat, fibre or protein;

(3) A pharmaceutical composition or dietary supplement comprising (I) and a carrier;

(4) A kit comprising (a) and the antioxidant source for separate, sequential or simultaneous administration; and

(5) A cosmetic composition comprising (a), the antioxidant source and a cosmetic base.

ACTIVITY - Antiarteriosclerotic; Antirheumatic; Cytostatic; Cardiant; Antiinflammatory; Virucide; Hepatotropic; Antialcoholic; Nootropic; Neuroprotective; Antidiabetic; Anti-HIV; Ophthalmological; Vasotropic; Virucide; Antipsoriatic; Dermatological; Antiseborrheic; and Cerebroprotective.

MECHANISM OF ACTION - Low density lipoprotein (LDL) oxidation suppressor.

USE - As a scavenger of free radicals; as a preservative for preventing spoilage of food and beverage products; as a medicament in the manufacture of medicament or nutritional formulation for the prevention or treatment of a disease condition (including arteriosclerosis, rheumatism or cancer) or corporal damage (caused by physical activity, exposure to the sun or smoking) associated with the generation of free radicals (all claimed); for treating any diseases associated with free radical damage (especially damage resulting in lipid peroxidation) for e.g. coronary heart disease (CHD), inflammation, hepatitis, alcoholism, Alzheimer's disease, dementia, diabetes, multiple sclerosis, HIV and AIDS, collagen degradation, cataracts, macular degeneration, accelerated aging,

neuropathies, myopathies, **ischemia**-reperfusion injury, haemorrhagic shock, gum disease, cold sores, psoriasis, eczema, seborrhea, cardiant infarct, and stroke; as a cosmetic treatment method to counteract the development of wrinkles, delay skin aging, and improve the overall appearance of skin, eyes and hair. Also useful to counteract the effects of formation of reactive oxygen species including that resulting from environmental pollution or irradiation and from treatment with neoplastic drugs.

ADVANTAGE - (I) is a potent synergic antioxidant combination for preventing diseases associated with free radical generation, at dosages which do not pose health risks. The composition supports and supplements the endogenous alpha -tocopherol antioxidant activity in diverse sites and tissue around the body.

Dwg.0/5

L112 ANSWER 26 OF 36 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-362323 [39] WPIDS
DOC. NO. CPI: C2002-102560
TITLE: Treating e.g. oxidative stress, cancer, autoimmune diseases, using compositions relating to hydrogen peroxide and superoxide production by antibodies, for.
DERWENT CLASS: B04 B05 D16
INVENTOR(S): JANDA, K D; JONES, L H; LERNER, R A; WENTWORTH, A D; WENTWORTH, P
PATENT ASSIGNEE(S): (SCRI) SCRIPPS RES INST
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002022573	A2	20020321	(200239)*	EN	103

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002012970 A 20020326 (200251)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002022573	A2	WO 2001-US29165	20010917
AU 2002012970	A	AU 2002-12970	20010917

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002012970	A Based on	WO 200222573

PRIORITY APPLN. INFO: US 2001-315906P 20010829; US 2000-232702P 20000915; US 2000-235475P 20000926

AB WO 200222573 A UPAB: 20020621

NOVELTY - Using an antioxidant to treat a cell to reduce antibody mediated generation of superoxide (SO) or hydrogen peroxide (HP) in the cell; or to treat oxidative stress in a subject, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) exposing an antigen to SO or HP comprises contacting the antigen with an antibody capable of generating SO or HP from singlet oxygen;

(2) inhibiting proliferation of a cancer cell, targeting or killing a

cancer cell, treating autoimmune diseases or wounds, by contacting the cells with an antibody capable of generating SO or HP from singlet oxygen;

(3) identifying an agent that modulates production of HP generated by antibody-mediated SO or HP generation by contacting an antibody capable of generating SO or HP from singlet oxygen with the agent in an assay solution in the presence of molecular oxygen irradiating the mixture; and detecting formed HP;

(4) an immunoassay to detect antibody immunoreactivity with an antigen;

(5) a therapeutic antioxidant comprising an engineered antibody molecule having less than 2 reductive centers, where production of SO or HP from singlet oxygen reduced by the reductive center is diminished;

(6) an engineered therapeutic antibody comprising at least 1 reductive center capable of reducing singlet oxygen to SO or HP;

(7) a method of detecting presence of an antigen in a bodily fluid by immobilizing a complex of the antigen with an antibody that is capable of generating SO or HP; and detecting SO or HP; and

(8) a composition comprising a T-cell receptor that can generate HP.

ACTIVITY - Cytostatic; Antiinflammatory; Nephrotropic; Dermatological; Immunosuppressive; Vasotropic; Cerebroprotective; Anti-HIV (human immunodeficiency virus); Antiulcer; Hypotensive; Gynecological; Neuroprotective; Nootropic; Antiparkinsonian; Vulnerary.

No biological data is given.

MECHANISM OF ACTION - Superoxide generation modulators; hydrogen peroxide generation modulators.

USE - The antibody mediated generation of SO or HP in a subject causes tissue injury, or is associated with an inflammatory condition (e.g. inflammation of the lungs), a disorder resulting from aberrant smooth muscle function, organ transplantation. The methods are useful for treating oxidative stress, e.g. in cancer, inflammatory diseases (arthritis, vasculitis, glomerulonephritis, systemic lupus erythematosus, adult respiratory distress syndrome), **ischemic** disease (heart disease, stroke, intestinal **ischemia**, reperfusion injury), hemochromatosis, acquired immunodeficiency syndrome, emphysema, organ transplantation, gastric ulcers, hypertension, preeclampsia, neurological disorders (multiple sclerosis, Alzheimer's disease, Parkinson's diseases, amyotrophic lateral sclerosis, muscular dystrophy), alcoholism and smoking-related diseases. The methods can be used for treating cancer cells, e.g. lung, prostate, colon, cervical, endometrial, bladder, bone or brain cancer, leukemia or lymphoma; treating autoimmune disease, and wound healing.

Methods are also used to detect the presence of an antigen, e.g. a drug or hormone, in a bodily fluid, e.g. blood or urine.

Dwg.0/13

L112 ANSWER 27 OF 36 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-061609 [08] WPIDS
DOC. NO. CPI: C2002-017532
TITLE: Use of desmethyl **tocopherol** such as **gamma tocopherol** for delaying or **preventing** cardiovascular disease.
DERWENT CLASS: B02
INVENTOR(S): FLOYD, R A; HENSLEY, K L
PATENT ASSIGNEE(S): (OKLA-N) OKLAHOMA MEDICAL RES FOUND
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2001044462	A1	20011122	(200208)*		13
US 6346544	B2	20020212	(200219)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2001044462	A1	Provisional	US 2000-186455P	20000302
			US 2001-794292	20010227
US 6346544	B2	Provisional	US 2000-186455P	20000302
			US 2001-794292	20010227

PRIORITY APPLN. INFO: US 2000-186455P 20000302; US 2001-794292 20010227

AB US2001044462 A UPAB: 20020204
NOVELTY - A method of delaying or preventing cardiovascular disease comprises use of at least one desmethyl **tocopherol** such as **gamma tocopherol**

ACTIVITY - Antiarteriosclerotic; cardiant; vasotropic; anticoagulant; thrombolytic.

MECHANISM OF ACTION - Platelet aggregation inhibitor.

Gamma-tocopherol was tested as inhibitor of platelet aggregation in vitro and in vivo, apparently through antagonism of protein kinase C (PKC). Platelets were stimulated to aggregate with ADP, thrombin receptor activating peptide (TRAP) or the PKC agonist phorbol myristyl acetate (PMA) and aggregation was measured. Specific platelets samples were preincubated with vehicle, alpha - **tocopherol** (500 ml) or **gamma -tocopherol** when tested for ability to inhibit PKC-linked platelet aggregation (e.g. when TRAP or PMA was used as the agonist). Results for **gamma - tocopherol** (50 micro M)/ alpha -tocopherol (500 micro M) showed platelet aggregation (% maximum) as 117/85 for ADP (20 micro M).

USE - For delaying or preventing symptoms and consequences of cardiovascular disease such as artherosclerosis, coronary artery disease or **ischemic** injury; for inhibiting cardiovascular damage resulting from thrombosis; and for preserving mitochondrial function in cardiovascular tissue (all claimed).

ADVANTAGE - The desmethyl tocopherol protects the cardiovascular tissue from nitratine stress.

Dwg.0/6

L112 ANSWER 28 OF 36 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2002-048610 [06] WPIDS
CROSS REFERENCE: 2000-302795 [26]; 2001-440358 [47]; 2003-182783 [18]
DOC. NO. CPI: C2002-013560
TITLE: Treatment of prostate cancer comprises **administering** composition containing specific amount of **gamma tocopherol**.
DERWENT CLASS: B02
INVENTOR(S): WECHTER, W J
PATENT ASSIGNEE(S): (WECH-I) WECHTER W J; (UYLO-N) UNIV LOMA LINDA MEDICAL CENT
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2001031782	A1	20011018	(200206)*		23
US 6410589	B1	20020625	(200246)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2001031782	A1	Cont of	US 1998-215608	19981217
		Cont of	US 1999-461645	19991214

			US 2001-814330	20010321
US 6410589	B1	Cont of	US 1998-215608	19981217
		Cont of	US 1999-461645	19991214
			US 2001-814330	20010321

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 2001031782	A1	Cont of	US 6048891
		Cont of	US 6242479
US 6410589	B1	Cont of	US 6048891
		Cont of	US 6242479

PRIORITY APPLN. INFO: US 1998-215608 19981217; US 1999-461645 19991214; US 2001-814330 20010321

AB US2001031782 A UPAB: 20030317

NOVELTY - Treatment of prostate cancer comprises administering a composition comprising tocopherols containing at least 50% **gamma -tocopherols.**

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a medicament comprising more than 70% **gamma -tocopherols**

.

ACTIVITY - Cytostatic; Antiarteriosclerotic; Hypotensive; Vasotropic; Hepatotropic; Cardiant; Nephrotropic; Immunostimulant; Uropathic.

Groups of mice were used in a study. Group 1 consisted of control mice in which tumor formation was not induced but **treatment** with a formulation of **gamma -tocopherol** (I) (75 wt.%) and 6-hydroxy-2,7,8-trimethylchroman-2-propanoic acid (LLU- alpha) (II) (25 wt.%) was rendered. Group 2 consisted of control mice in which tumor formation was induced and treatment was not rendered. Group 3 consisted of experimental mice in which tumor formation was induced and treatment with formulation of (I) (75 wt.%) and LLU- alpha (25 wt.%) was rendered. Mice which received treatment with (I) or the formulation of (I) and (II) as above were given 20 mg/kg of supplement for a period of 2-4 weeks. Tumor cells derived from a spontaneously arising mammary tumor were then injected into the thigh area of the experimental mice to induce tumor formation. Treatment with (I) and the formulation was continued according the protocol.

After 21 days, the mean volume of tumors in the mice were determined and compared. The results of this study demonstrated that the mean volume of tumor in the mice treated with (I) and the formulation of (I) and (II), was less than the mean volume of tumors in the control mice in which tumor formation was induced, but (I) or the formulation of (I) and (II) was not administered.

MECHANISM OF ACTION - None given in source material.

USE - Used for treating prostate cancer (claimed), high blood pressure, thromboembolic disease, artherosclerosis, natriuretic disease such as hypertension, **ischemia**, angina pectoris, congestive least failure, cirrhosis of the liver, nephrotic syndrome, ineffective renal perfusion, and ~~ineffective~~ glomerular filtration, cardiovascular disease, the formation of neuropathological lesions and reduced immune system response.

ADVANTAGE - The method improves immune system response and reduces the production of free radicals and thus provides therapeutic benefits. Dwg.0/0

L112 ANSWER 29 OF 36 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-440358 [47] WPIDS
CROSS REFERENCE: 2000-302795 [26]; 2002-048610 [06]; 2003-182783 [18]
DOC. NO. CPI: C2001-132934
TITLE: Treating cardiovascular disease, cancer and neurological disease and improving immune response comprises oral or

parenteral administration of tocopherol composition.
DERWENT CLASS: B02
INVENTOR(S): WECHTER, W J
PATENT ASSIGNEE(S): (UYLO-N) UNIV LOMA LINDA MEDICAL CENT
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6242479	B1	20010605	(200147)*		22

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6242479	B1 Cont of	US 1998-215608	19981217
		US 1999-461645	19991214

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 6242479	B1 Cont of	US 6048891

PRIORITY APPLN. INFO: US 1998-215608 19981217; US 1999-461645 19991214
AB US 6242479 B UPAB: 20030317
NOVELTY - Treating or preventing cardiovascular disease, cancer and neurological disease and improving immune response comprise orally or parenterally administering a composition comprising tocopherols. At least 50% of the **tocopherols** are **gamma -tocopherol**

ACTIVITY - Anticoagulant; thrombolytic; antiarteriosclerotic; antilipemic; vasotropic; cytostatic; neuroprotective; immunostimulant; hypotensive; antianginal; hepatotropic; nephrotropic; ophthalmological; cardiant.

MECHANISM OF ACTION - None given.

USE - Used for treating cardiovascular disease, particularly thromboemoblic disease, atherosclerosis, low-density lipid oxidation, adhesion of monocytes to endothelial cells, foam-cell formation, fatty streak development, platelet adherence, platelet aggregation, smooth muscle cell proliferation and reperfusion injury, cancer including lung cancer, prostate cancer, breast cancer and colon cancer, and neurological disease including hyporeflexia, proprioception, opthalmoplegia and axonal dystrophy, and to improve an immune response including reduced prostaglandin E2 production, increased mitogenic response, increased interleukin-2 production and induction of delayed-type hypersensitivity. The method is also used to treat natriuretic disease, such as high blood pressure, hypertension, **ischemia**, angina pectoris, congestive heart failure, cirrhosis of the liver, nephrotic syndrome, ineffective renal perfusion, or ineffective glomerular filtration, and the formation of neuropathological lesions.

ADVANTAGE - The methods provide combined **treatment** with **gamma -tocopherol** and LLU- alpha , selectively providing natriuretic redox agents to the lipid and aqueous phases of the body. Dwg.0/0

L112 ANSWER 30 OF 36 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2001-337647 [36] WPIDS
DOC. NO. CPI: C2001-104594
TITLE: Preparation of tocopherol ascorbic acid-2-diethylphosphates, by reaction of tocopherol and halophosphorates in the presence of a base in a

hydrophilic solvent.
DERWENT CLASS: B02
PATENT ASSIGNEE(S): (SENP) SENJU SEIYAKU KK
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 2001002690	A	20010109	(200136)*		5

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 2001002690	A	JP 1999-170578	19990617

PRIORITY APPLN. INFO: JP 1999-170578 19990617
AB JP2001002690 A UPAB: 20010628
NOVELTY - A new preparation of tocopherol ascorbic acid-2-diethylphosphates (I) comprises reaction of tocopherol and halophosphorates in the presence of a base in a hydrophilic solvent and optional deprotection.
DETAILED DESCRIPTION - Diethyl phosphates of formula (I) or their pharmacologically acceptable salts are prepared by reaction of compounds (obtainable by reaction of alpha-, **beta-**, **gamma-**, or **delta-tocopherol** with halophosphoric acid esterifying agents) with ascorbic acid in a hydrophilic solvent in the presence of a 3-equivalent amount of an alkali metal hydroxide, carbonate, or tertiary amine followed by removal of the protecting group if the hydroxy groups at 5- and 6-positions in ascorbic acid are protected:
R1, R2 = differently H or Me.
ACTIVITY - Gynecological; opthalmological; vasotropic; antioxidant; antiulcer; antiinflammatory.
MECHANISM OF ACTION - Maillard reaction inhibitor.
USE - The phosphates prepared are useful in the prevention and treatment of cataract, menopausal disorders, and **ischemic** organ diseases; or useful as hypopigmenting cosmetics, antioxidants, antiulcers, antiinflammatory agents, and Maillard reaction inhibitory agents.
ADVANTAGE - The method has shorter chemical processes and higher yields when compared to prior-art methods for the preparation of the phosphates.
Dwg.0/0

L112 ANSWER 31 OF 36 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 2000-374331 [32] WPIDS
CROSS REFERENCE: 2001-272595 [28]
DOC. NO. CPI: C2000-113143
TITLE: Water-soluble composition used for treating e.g. cardiovascular diseases comprises bioactive lipophilic compound, especially coenzyme Q10 and solubilizing agent.
DERWENT CLASS: A96 B05 B07
INVENTOR(S): BOROWY-BOROWSKI, H; SIKORSKA-WALKER, M; WALKER, R P; WALKER, P R
PATENT ASSIGNEE(S): (CANA) NAT RES COUNCIL CANADA
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6045826	A	20000404	(200032)*		19
WO 2000061189	A2	20001019	(200054)	EN	

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000022734 A 20001114 (200108)
EP 1159006 A2 20011205 (200203) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
BR 2000009532 A 20011226 (200206)
NO 2001004780 A 20011127 (200208)
FI 2001001914 A 20011119 (200215)
SK 2001001393 A3 20020509 (200239)
CZ 2001003462 A3 20020612 (200251)
KR 2002012167 A 20020215 (200257)
CN 1352568 A 20020605 (200261)
HU 2002000796 A2 20020828 (200264)
JP 2002541216 W 20021203 (200309) 65
ZA 2001008061 A 20030326 (200327) 97

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6045826	A	US 1999-285244	19990402
WO 2000061189	A2	WO 2000-CA76	20000203
AU 2000022734	A	AU 2000-22734	20000203
EP 1159006	A2	EP 2000-901445	20000203
		WO 2000-CA76	20000203
BR 2000009532	A	BR 2000-9532	20000203
		WO 2000-CA76	20000203
NO 2001004780	A	WO 2000-CA76	20000203
		NO 2001-4780	20011001
FI 2001001914	A	WO 2000-CA76	20000203
		FI 2001-1914	20010928
SK 2001001393	A3	WO 2000-CA76	20000203
		SK 2001-1393	20000203
CZ 2001003462	A3	WO 2000-CA76	20000203
		CZ 2001-3462	20000203
KR 2002012167	A	KR 2001-712544	20010929
CN 1352568	A	CN 2000-808089	20000203
HU 2002000796	A2	WO 2000-CA76	20000203
		HU 2002-796	20000203
JP 2002541216	W	JP 2000-610521	20000203
		WO 2000-CA76	20000203
ZA 2001008061	A	ZA 2001-8061	20011001

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000022734	A	Based on	WO 200061189
EP 1159006	A2	Based on	WO 200061189
BR 2000009532	A	Based on	WO 200061189
SK 2001001393	A3	Based on	WO 200061189
CZ 2001003462	A3	Based on	WO 200061189
HU 2002000796	A2	Based on	WO 200061189
JP 2002541216	W	Based on	WO 200061189

PRIORITY APPLN. INFO: US 1999-285244 19990402
AB US 6045826 A UPAB: 20030429
NOVELTY - Water soluble composition (A) comprises a bioactive lipophilic compound and a solubilizing agent (I).

DETAILED DESCRIPTION - Water soluble composition (A) comprises a bioactive lipophilic compound and a solubilizing agent of formula (X-OOC-((CH2)n-COO)m)p-Y (I).

X = a residue of a hydrophobic sterol, tocopherol or their derivatives;

Y = a residue of a hydrophilic polyether, polyalcohol or their derivatives;

p = 1 or 2;

m = 0 or 1 and

n = 0-18,

provided that when p and m are 1 and the hydrophobic group is cholesterol, n is between 4 and 8 and when p and m are 1 and the hydrophobic group is (+)- alpha -tocopherol, n is not 2.

INDEPENDENT CLAIMS are included for the following:

(1) preparation of (A) which comprises heating a mixture of the lipophilic compound and (I) in a predetermined molar ratio to give a clear melt and recovering (A);

(2) preparation of (A) which comprises dissolving the lipophilic compound and (I) in a predetermined molar ratio in a water soluble organic solvent, diluting the solution with water and removing the organic solvent and optionally water solution of the lipophilic compound and solubilizing agent with water and removing the solvent;

(3) purifying a water soluble composition which comprises dissolving the composition in not more than 2 volumes of water, heating the solution to separate the water-soluble composition as a liquid phase and separating the liquid phase from the hot solution while maintaining the temperature unchanged;

(4) a pharmaceutical or cosmetic composition comprising a bioactive lipophilic compound in the form of (A) and an additive or vehicle comprising solvents, adjuvants, sweeteners, fillers, flavorants, lubricants, binders, moisturizing agents and/or preservatives;

(5) treatment of a medical disorder associated with oxidative tissue damage or mitochondrial dysfunction which comprises administration of (A) containing coenzyme Q10 as the lipophilic compound;

(6) treating a fungal infection which comprises administration of (A) comprising a macrolide polyene antibiotic as the lipophilic compound and

(7) preparation of a water soluble composition of coenzyme Q10 which comprises dissolving coenzyme Q10 in (I).

USE - Useful for treating disorders related to tissue damage caused by free radicals and oxidants and/or mitochondrial dysfunction including cardiovascular diseases, muscular disorders, mitochondrial encephalomyolopathies and neurodegenerative disorders, restoration of immune deficiencies caused by drugs or infections and minimizing tissue damage resulting from **ischemia** and reperfusion. The coenzyme Q10 is also used as an adjuvant for treating infectious diseases, in combination with cholesterol lowering agents for treating hypercholesteremia, in combination with chemotherapeutic agent for treating cancers and in cosmetics for slowing skin ageing.

Dwg.0/5

L112 ANSWER 32 OF 36 WPIDS (C) 2003 THOMSON DERWENT
ACCESSION NUMBER: 1997-512404 [47] WPIDS
DOC. NO. CPI: C1997-163513
TITLE: Unit dosage form for treatment of vasoconstriction - comprises magnesium, tocopherol, ascorbic acid or ascorbate, folic acid or folate, and selenium.
DERWENT CLASS: B05
INVENTOR(S): PEARSON, D C; RICHARDSON, K T
PATENT ASSIGNEE(S): (RICH-N) RICHELL LAB LLC; (CHRO-N) CHRONORX LLC
COUNTRY COUNT: 76
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 9737670 A1 19971016 (199747)* EN 24
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU
AU 9725833 A 19971029 (199810)
US 5849338 A 19981215 (199906)
US 6042849 A 20000328 (200023)

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9737670	A1		WO 1997-US4286	19970318
AU 9725833	A		AU 1997-25833	19970318
US 5849338	A	CIP of	US 1996-753967	19961204
			WO 1997-US4286	19970318
			US 1997-849068	19970826
US 6042849	A	Provisional	US 1996-15115P	19960410
		CIP of	US 1996-753967	19961204
		Cont of	WO 1997-US4286	19970318
		Cont of	US 1997-849068	19970826
			US 1998-111055	19980707

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9725833	A	Based on	WO 9737670
US 5849338	A	Based on	WO 9737670

PRIORITY APPLN. INFO: US 1996-753967 19961204; US 1996-15115P 19960410; US 1997-849068 19970826; US 1998-111055 19980707

AB WO 9737670 A UPAB: 19971125
A unit dosage form for treatment of vasoconstriction and physiological conditions giving rise thereto, comprises a combination of: (i) magnesium; (ii) one of alpha -**tocopherol**, **beta** -**tocopherol**, and their esters; (iii) ascorbic acid or ascorbate ion; (iv) folic acid or folate ion; and (v) selenium.

The Mg is supplied in the form of Mg lactate, Mg citrate, Mg stearate, Mg acetate, Mg ascorbate, Mg malate, Mg orotate, Mg diglycinate and/or Mg oxide. (ii) is alpha -tocopherol, alpha -tocopherol acid succinate or alpha -tocopherol acetate. The dosage form is a tablet, gelatin capsule, solution, suspension or powder.

USE - Used for treatment of vasoconstriction, which is caused by magnesium deficiency. The dosage form reduces risk factors for diseases negatively influenced by vasospasm and other forms of vasoconstriction or abnormal vasodilation, such as diabetic retinopathy, migraine, peripheral vascular disease, disorders of the microcirculation of the optic nerve, low tension or normal tension glaucoma, chronic open angle or primary open angle glaucoma, coronary artery disease, **ischaemic** heart disease, **ischaemic** cerebrovascular disease and systemic hypertension, by the action of elemental Mg as a physiological calcium channel blocker and its action in reducing activating factors involved in the production of inflammatory, vasospastic cytokines.
Dwg.0/0

L112 ANSWER 33 OF 36 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 1999:427630 SCISEARCH
THE GENUINE ARTICLE: 201KG

TITLE: gamma-Tocopherol decreases ox-LDL-mediated activation of nuclear factor-kappa B and apoptosis in human coronary artery endothelial cells
AUTHOR: Li D U; Saldeen T; Mehta J L (Reprint)
CORPORATE SOURCE: UNIV FLORIDA, COLL MED, DEPT MED, 1600 ARCHER RD, POB 100277 JHMHC, GAINESVILLE, FL 32610 (Reprint); UNIV FLORIDA, COLL MED, DEPT MED, GAINESVILLE, FL 32610; UNIV FLORIDA, DEPT PHYSIOL, GAINESVILLE, FL 32610; VET AFFAIRS MED CTR, GAINESVILLE, FL 32608; UPPSALA UNIV, DEPT FORENS MED, UPPSALA, SWEDEN
COUNTRY OF AUTHOR: USA; SWEDEN
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (27 MAY 1999) Vol. 259, No. 1, pp. 157-161.
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 0006-291X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 38
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB gamma-Tocopherol, produced by many plants, is the major form of tocopherol in the United States diet. It is an effecient protector of lipids against peroxidative damage. Epidemiologic studies show that supplementation of diet with gamma-tocopherol is inversely related to the risk of death from cardiovascular disease. This study was conducted to examine the role of gamma-tocopherol in oxidized LDL (ox-LDL)-induced nuclear factor (NF)-kappa B activation and apoptosis in human coronary artery endothelial cells (HCAECs). Cultured HCAECs were treated with ox-LDL (10-40 mu g/ml). Incubation of HCAECs with ox-LDL resulted in apoptosis of HCAECs, as determined by TUNEL and DNA laddering. Ox-LDL degraded I kappa B protein and activated NF-kappa B in HCAECs (both $P < 0.01$ vs control), as determined by Western blot. **Treatment** of cells with **gamma-tocopherol** attenuated ox-LDL-mediated degradation of I kappa B and activation of NF-kappa B (both $P < 0.01$ vs ox-LDL alone). The presence of gamma-tocopherol also reduced ox-LDL-induced apoptosis ($P < 0.01$ vs ox-LDL alone). A high concentration of gamma-tocopherol (50 mu mol/L) was more effective than the low concentration of gamma-tocopherol (10 mu mol/L) in this process. These observations show that ox-LDL induces apoptosis of HCAECs at least partially by activation of NF-kappa B signal transduction pathway. gamma-Tocopherol significantly decreases ox-LDL-induced apoptosis of HCAECs by inhibiting the activation of NF-kappa B. (C) 1999 Academic Press.

L112 ANSWER 34 OF 36 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 96:3231 SCISEARCH
THE GENUINE ARTICLE: TK019
TITLE: VITAMIN-E - A SENSOR AND AN INFORMATION TRANSDUCER OF THE CELL OXIDATION-STATE
AUTHOR: AZZI A (Reprint); BOSCOBOINIK D; MARILLEY D; OZER N K; STAUBLE B; TASINATO A
CORPORATE SOURCE: UNIV BERN, INST BIOCHEM & MOLEK BIOL, BUHLSTR 28, CH-3012 BERN, SWITZERLAND (Reprint)
COUNTRY OF AUTHOR: SWITZERLAND
SOURCE: AMERICAN JOURNAL OF CLINICAL NUTRITION, (DEC 1995) Vol. 62, No. 6, Supp. S, pp. S1337-S1346.
ISSN: 0002-9165.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 82
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We studied the effects of RRR-alpha-tocopherol and RRR-beta-tocopherol in smooth muscle cells from rat (line A7r5) and human aortas. RRR-alpha-Tocopherol, but not RRR-beta-tocopherol, inhibited smooth muscle cell proliferation in a dose-dependent manner at concentrations in the range from 10 to 50 mu mol/L. RRR-beta-Tocopherol added simultaneously with RRR-alpha-tocopherol prevented growth inhibition. The earliest event brought about by RRR-alpha-tocopherol in the signal transduction cascade controlling receptor-mediated cell growth was the activation of the transcription factor AP-1. RRR-beta-tocopherol alone was without effect but in combination with RRR-alpha-tocopherol prevented the AP-1 activating effect of the latter. Protein kinase C was inhibited by RRR-alpha-tocopherol and not by RRR-**beta-tocopherol**, which also in this case **prevented** the effect of RRR-alpha-tocopherol. Calyculin A, a protein phosphatase inhibitor, prevented the effect of RRR-alpha-tocopherol on protein kinase C. The data can be rationalized by a model in which a tocopherol-binding protein discriminates between RRR-alpha-tocopherol and RRR-beta-tocopherol and initiates a cascade of events at the level of cell signal transduction that leads to the inhibition of cell proliferation.

L112 ANSWER 35 OF 36 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 95:415114 SCISEARCH
THE GENUINE ARTICLE: RC514
TITLE: FATTY-ACID COMPOSITION OF CHOLESTEROL ESTERS AND SERUM TOCOPHEROLS IN MELANESIANS APPARENTLY FREE FROM CARDIOVASCULAR-DISEASE - THE KITAVA STUDY
AUTHOR: LINDEBERG S (Reprint); VESSBY B
CORPORATE SOURCE: LUND UNIV, DEPT COMMUNITY HLTH SCI, S-22354 LUND, SWEDEN (Reprint)
COUNTRY OF AUTHOR: SWEDEN
SOURCE: NUTRITION METABOLISM AND CARDIOVASCULAR DISEASES, (1995) Vol. 5, No. 1, pp. 45-53.
ISSN: 0939-4753.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: No References Keyed
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Fatty acid (FA) composition of cholesterol esters (CE) and serum tocopherols were measured in 168 subsistence horticulturalists of Kitava, Trobriand Islands, Papua New Guinea, whose diet consists of tubers, fruit, coconut, fish and vegetables with a negligible influence of western food. Stroke and **ischaemic** heart disease (IHD) appear to be absent despite high smoking rates and intermediate serum lipoprotein levels. Comparisons were made with serum samples from healthy Swedish subjects, randomly selected from employees of a telephone company. A dietary survey was made in Kitava including diet history and weighing of constituents of ready-to-eat portions. The percentages of all CE-FAs except arachidonic and oleic acid differed markedly between the two populations. Kitavans had higher saturated FAs while polyunsaturated FAs (PUFAs) were lower. Lauric acid was only detectable in trace amounts despite a very high estimated intake in Kitava. In spire of a lower intake, palmitic acid was higher in Kitavans, possibly reflecting endogenous fat synthesis due to low total fat intake. Marine n-3 PUFAs were much higher while linoleic acid was much lower in Kitavans. Alpha tocopherol was slightly higher in Kitavan than in Swedish males, while it did not differ among females. **Gamma Tocopherol** was much lower in Kitavans. In conclusion, the high intake of marine n-3 PUFAs and the high n-3/n-6 ratio may partially explain the apparent absence of IHD in Kitava, while serum tocopherols in this study seem of little importance.

L112 ANSWER 36 OF 36 SCISEARCH COPYRIGHT 2003 THOMSON ISI
ACCESSION NUMBER: 94:393447 SCISEARCH

THE GENUINE ARTICLE: NT095
TITLE: EFFECTS OF SELENIUM AND ALPHA-TOCOPHEROL ON LIVER-DAMAGE INDUCED BY FEEDING GRAINS FROM AN ENDEMIC AREA OF KESHAN-DISEASE IN RATS
AUTHOR: LIU S Y (Reprint); LI T Y; ZHAO Z T; MAN R Y K; WANG F
CORPORATE SOURCE: UNIV MANITOBA, FAC MED, DEPT PHARMACOL & THERAPEUT, WINNIPEG R3E 0W3, MB, CANADA (Reprint); NORMAN BETHUNE UNIV MED SCI, INST PRECLIN SCI, CHANGCHUN, PEOPLES R CHINA
COUNTRY OF AUTHOR: CANADA; PEOPLES REPUBLIC OF CHINA
SOURCE: MOLECULAR AND CELLULAR BIOCHEMISTRY, (30 MAR 1994) Vol. 132, No. 2, pp. 109-115.
ISSN: 0300-8177.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 21

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Previous studies have shown the pathogenic effects of grains cultivated in the endemic areas of Keshan disease and selenium is effective in the prevention of this disease. In this study, liver damages induced by feeding grains from an endemic area (endemic diet), and the effects of selenium and alpha-tocopherol supplement were examined. After 3 months on the endemic diet, the amounts of serum enzymes were significantly increased when compared to controls (animals receiving diet from a non-endemic area). Liver enzymes (alkaline phosphatase and choline esterase) were also found to be altered in the serum, further suggesting liver damages in animals on an endemic diet. Supplement of the endemic diet with selenium or alpha-tocopherol reversed the changes in serum enzymes. Increase in lipid peroxidation in the liver of animals on the endemic diet was observed when compared to that in control animals. Selenium and alpha-tocopherol supplements prevented the increase in lipid peroxidation in the liver by the endemic diet. Semi-quantitative histochemical analysis of glutamate dehydrogenase and succinate dehydrogenase in liver tissue showed that the livers of animals on an endemic diet were more sensitive to **ischemic** damages in vitro. Supplementation of the endemic diet with either selenium or alpha-tocopherol reduced the sensitivity to **ischemic** damages. The results suggest that increased lipid peroxidation in the liver of rats on an endemic diet may be responsible for liver damages and elevation of serum enzymes. Restoration of glutathione peroxidase activity by selenium supplement or an increase in the content of alpha-tocopherol in the liver can prevent lipid peroxidation in animals on an endemic diet and thus provide the protective effects against liver damages.

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=> fil medl; d que l66
FILE 'MEDLINE' ENTERED AT 10:32:37 ON 22 MAY 2003

 FILE LAST UPDATED: 21 MAY 2003 (20030521/UP). FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L40      277250 SEA FILE=MEDLINE ABB=ON  ISCHEMIA+NT/CT
L50       60735 SEA FILE=MEDLINE ABB=ON  L40(L)(DT OR PC)/CT
L60        3264 SEA FILE=MEDLINE ABB=ON  DIOSMIN/CT OR RUTIN+NT/CT OR QUERCETIN
               +NT/CT OR HESPERIDIN/CT
L61        1504 SEA FILE=MEDLINE ABB=ON  CHRYSIN OR DAIDZEIN OR HESPERETIN OR
               LUTEOLIN OR BROMOQUERCETIN OR BIOCHANIN
L62          59 SEA FILE=MEDLINE ABB=ON  (L60 OR L61) AND L50
L66          10 SEA FILE=MEDLINE ABB=ON  GENERAL REVIEW/DT AND L62
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Review articles discussing use of compounds in 4) to treat ischemia (not in combination w/ tocopherols)

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=> d ibib ab 166 1-10; fil hom

L66  ANSWER 1 OF 10     MEDLINE
ACCESSION NUMBER:    2002340025     MEDLINE
DOCUMENT NUMBER:     22078164   PubMed ID: 12083462
TITLE:               Anti-inflammatory actions of a micronized, purified
                     flavonoid fraction in ischemia/reperfusion.
AUTHOR:              Korthui Ronald J; Gute Dean C
CORPORATE SOURCE:    Department of Molecular and Cellular Physiology, Louisiana
                     State University Health Sciences Center, School of Medicine
                     in Shreveport, 71130, USA.. rkorth@lsuhsc.edu
CONTRACT NUMBER:     DK-43785 (NIDDK)
     HL-54797 (NHLBI)
SOURCE:              ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (2002) 505
                     181-90.  Ref: 21
                     Journal code: 0121103. ISSN: 0065-2598.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
                       General Review; (REVIEW)
                     (REVIEW, TUTORIAL)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200301
ENTRY DATE:          Entered STN: 20020627
                     Last Updated on STN: 20030111
                     Entered Medline: 20030110
AB   It is now recognized that reperfusion after a prolonged period of reduced
     or absent blood flow, although necessary to salvage ischemic tissue,
     initiates a complex series of deleterious reactions which ultimately
     induce the same effects as ischemia per se, i.e., cell injury and
     necrosis. Work conducted over the past 15 years has uncovered the fact
     that post-ischemic leukocyte infiltration plays a major role in the
     reperfusion component of ischemia/reperfusion (I/R) injury. This
     discovery has led to a concerted research effort directed at identifying
     interventions that prevent post-ischemic leukocyte adhesion and
     emigration. Recent work indicates that flavonoids are particularly
     effective anti-inflammatory agents in the setting of I/R. While the
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mechanisms underlying the powerful protective effects of these compounds is uncertain, a growing body of evidence indicates that flavonoids are potent anti-oxidants that also act to inhibit the activity of key regulatory enzymes involved in the activation of pro-inflammatory signaling cascades. In addition, it appears that these compounds prevent the expression of specific adhesion molecules involved in leukocyte recruitment, observations which provide the molecular basis for the anti-adhesive properties of these compounds.

L66 ANSWER 2 OF 10 MEDLINE
ACCESSION NUMBER: 2001129427 MEDLINE
DOCUMENT NUMBER: 21038386 PubMed ID: 11187733
TITLE: Phytoestrogens.
AUTHOR: Kinjo J
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Fukuoka University.
SOURCE: NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (2000 Dec) 58 (12) 2434-8. Ref: 20
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301

AB Epidemiological studies revealed that foodstuffs, in particular, soy foods containing isoflavonoid phytoestrogens may reduce the risk of some hormone-dependent disease such as not only postmenopausal symptoms but also certain(breast, prostate and colon) cancers and cardiovascular disease. This review introduces the metabolism of soybean isoflavonoids by human intestinal bacteria and the binding and gene-expression activity of the metabolites towards the human estrogen receptor(hER) alpha and beta. The dietary isoflavones(daidzin and genistin) in soybean were metabolized to equol and dihydrogenistein via **daidzein** and genistein, respectively. The metabolites bind more strongly to hER beta than hER alpha. The binding affinity of genistein is comparable that of 17 beta-estradiol. Equol induces transcription most strongly both with hER beta and hER alpha.

L66 ANSWER 3 OF 10 MEDLINE
ACCESSION NUMBER: 2000269719 MEDLINE
DOCUMENT NUMBER: 20269719 PubMed ID: 10807939
TITLE: Dietary soy-derived isoflavone phytoestrogens. Could they have a role in coronary heart disease prevention?.
AUTHOR: Tikkanen M J; Adlercreutz H
CORPORATE SOURCE: Department of Medicine, Helsinki University Central Hospital, 00290 Helsinki, Finland..
matti.j.tikkanen@helsinki.fi
SOURCE: BIOCHEMICAL PHARMACOLOGY, (2000 Jul 1) 60 (1) 1-5. Ref: 38
Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000629
Last Updated on STN: 20000629
Entered Medline: 20000616

AB Soy protein-containing foods are a rich source of isoflavone phytoestrogens, such as genistein and **daidzein**. There is great interest in these substances, as lower rates of chronic diseases, including coronary heart disease, have been associated with high dietary intake of soy-containing foods. Soy phytoestrogens bind weakly to estrogen receptors, and some bind more strongly to estrogen receptor-beta compared with estrogen receptor-alpha. A meta-analysis has indicated that isoflavone phytoestrogens lowered plasma cholesterol concentrations in subjects with initially elevated levels, but had little effect in subjects with normal cholesterol concentrations. These substances reportedly may also have beneficial effects on arterial endothelial function. In addition to these potentially antiatherogenic effects, many laboratories are investigating other possible mechanisms, including antioxidative and antiproliferative properties of these substances. We have shown that dietary supplementation with soy-derived isoflavones reduced the in vitro oxidation susceptibility of low-density lipoprotein (LDL). To further explore this phenomenon, we incorporated genistein and **daidzein** into LDL molecules in vitro with the aid of an artificial transfer system. However, it was necessary to convert the isoflavone molecules to fat-soluble derivatives, fatty acid esters (analogous to esterified endogenous estrogens, which are known to occur in vivo), to achieve significant incorporation. The LDLs containing esterified isoflavones were shown to be less susceptible to oxidation in vitro than native LDL. We also employed U937 cell cultures for investigating the effects of isoflavone-containing LDLs on cell proliferation. Some of these LDLs exhibited antiproliferative effects in cultured U937 cells. In summary, lipophilic phytoestrogen derivatives could be incorporated into LDLs, increasing their oxidation resistance and antiproliferative efficacy ex vivo, both of which are, in theory, antiatherogenic effects. Further studies are needed to assess to what extent analogous effects could be produced in vivo and whether such substances have a role in hormone replacement and coronary heart disease prevention in postmenopausal women.

L66 ANSWER 4 OF 10 MEDLINE
ACCESSION NUMBER: 1998135906 MEDLINE
DOCUMENT NUMBER: 98135906 PubMed ID: 9477039
TITLE: Postischemic leukocyte/endothelial cell interactions and microvascular barrier dysfunction in skeletal muscle: cellular mechanisms and effect of Daflon 500 mg.
AUTHOR: Korthuis R J; Gute D C
CORPORATE SOURCE: Department of Physiology, Louisiana State University Medical Center, School of Medicine in Shreveport, 71130-3932, USA.. rkorth@lsumc.edu
SOURCE: INTERNATIONAL JOURNAL OF MICROCIRCULATION: CLINICAL AND EXPERIMENTAL, (1997) 17 Suppl 1 11-7. Ref: 24
Journal code: 8400122. ISSN: 0167-6865.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980410
Last Updated on STN: 19980410
Entered Medline: 19980402

AB A growing body of evidence indicates that neutrophils play a critical role in disrupting the microvascular barrier in skeletal muscle. Recent studies from our laboratory and by others indicate that administration of antibodies directed against P-selectin, ICAM-1, or the common subunit ~~(CD18) of CD11~~/CD18 was as effective as neutrophil depletion in attenuating ischemia/reperfusion ~~(I~~/R)-induced microvascular barrier ~~disruption and edema formation in~~ skeletal muscle. These studies have

important implications with regard to the pathogenesis of leg ulceration in view of our more recent work indicating that the increase in tissue pressure induced by edema formation secondary to microvascular barrier disruption may lead to the development of capillary no-reflow. The resulting maldistribution of blood flow during reperfusion exacerbates muscle injury ~~induced~~ by ischemia. Daflon 500 mg is a purified, micronized flavonoid fraction that exhibits a number of anti-inflammatory properties ~~and is used~~ clinically to treat venous insufficiency. In view of these actions and the demonstrated role of neutrophil adhesion in the pathogenesis of I/R, we sought to determine whether this agent would prevent leukocyte adhesion and microvascular barrier disruption in postischemic rat cremaster muscles and small bowel. Rats were treated with Daflon 500 mg (80 mg/kg/day by gavage) or its vehicle for 2 (cremaster studies) or 10 (mesenteric studies) days prior to the experiments. Leukocyte/endothelial cell interactions and venular protein leakage were quantitated using intravital microscopic techniques in rat cremaster muscles and mesenteries subjected to ischemia (60 min for cremaster, 20 min for mesentery) and reperfusion (60 min). The results indicated that Daflon 500 mg was as effective as the anti-adhesive monoclonal antibodies in reducing postischemic leukocyte adhesion and emigration and venular protein leakage in these models.

L66 ANSWER 5 OF 10 MEDLINE
ACCESSION NUMBER: 97409219 MEDLINE
DOCUMENT NUMBER: 97409219 PubMed ID: 9263608
TITLE: Natural and synthetic isoflavones in the prevention and treatment of chronic diseases.
AUTHOR: Brandi M L
CORPORATE SOURCE: Department of Clinical Physiopathology, University of Florence, Italy.
SOURCE: CALCIFIED TISSUE INTERNATIONAL, (1997) 61 Suppl 1 S5-8. Ref: 42
Journal code: 7905481. ISSN: 0171-967X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971105

AB The evidence that natural isoflavones protect against several chronic diseases is both observational and experimental. In humans, epidemiologic findings clearly show a higher incidence of some common types of cancer (i.e., breast, prostate, and colon) and of coronary heart diseases in Western populations exposed to limited amounts of soybean isoflavones (i.e., genistein, **daidzein**) in the diet. Further evidence for cancer and cardiac protection and antiatherogenic effects resulting from soybean isoflavones administration has been noted in various experimental animal models. Isoflavones may also prevent postmenopausal bone loss and osteoporosis. In fact, genistein has been reported to be as active as estrogens in maintaining bone mass in ovariectomized rats. Moreover, the synthetic isoflavone derivative ipriflavone is able to reduce bone loss in various types of animal models of experimental osteoporosis providing a rationale on its use in the prevention and treatment of postmenopausal and senile osteoporosis in humans. The mechanism through which isoflavones may exert the above-mentioned effects seems to depend, at least in part, on their mixed estrogen agonist-antagonist properties. An alternative hypothetical mechanism could derive from other biochemical actions of isoflavones such as inhibition of enzymatic activity, in particular protein kinases, or activation of an "orphan" receptor distinct from the

estrogen type I receptor.

L66 ANSWER 6 OF 10 MEDLINE
ACCESSION NUMBER: 97033101 MEDLINE
DOCUMENT NUMBER: 97033101 PubMed ID: 8878848
TITLE: Role of dietary flavonoids in protection against cancer and coronary heart disease.
AUTHOR: Hollman P C; Hertog M G; Katan M B
CORPORATE SOURCE: DLO State Institute for Quality Control of Agricultural products (RIKILT-DLO) Wageningen, The Netherlands.
SOURCE: BIOCHEMICAL SOCIETY TRANSACTIONS, (1996 Aug) 24 (3) 785-9. Ref: 29
Journal code: 7506897. ISSN: 0300-5127.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970306
Last Updated on STN: 19970306
Entered Medline: 19970226

L66 ANSWER 7 OF 10 MEDLINE
ACCESSION NUMBER: 96356464 MEDLINE
DOCUMENT NUMBER: 96356464 PubMed ID: 8748884
TITLE: Cellular basis of inflammation, edema and the activity of Daflon 500 mg.
AUTHOR: Friesenecker B; Tsai A G; Intaglietta M
CORPORATE SOURCE: Department of Anesthesiology and Intensive Care Medicine, University of Innsbruck, Austria.
SOURCE: INTERNATIONAL JOURNAL OF MICROCIRCULATION: CLINICAL AND EXPERIMENTAL, (1995) 15 Suppl 1 17-21. Ref: 44
Journal code: 8400122. ISSN: 0167-6865.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19961008
Last Updated on STN: 19961008
Entered Medline: 19960926

AB Inflammation activates leukocytes causing the release of agents that disrupt the endothelial barrier to such an extent that retention of plasma protein is impaired. This phenomenon can be observed using microvascular methods in which ischemia-reperfusion-induced inflammation-like condition are analyzed in terms of the increased adherence of leukocytes to the venular endothelium. Pretreatment with Daflon 500 mg, a purified, micronized, flavonoid fraction consisting of 90% diosmin and 10% hesperidin, prior to the induction of 4 h of tourniquet ischemia significantly lowers the number of adherent leukocytes. This observation is linked to the protective effect of flavonoids in the treatment of edema, as decreased activation is also associated with a decreased platelet and complement system activation, leading to a lowered release of histamine and decreased leukocyte-dependent endothelial damage. It is proposed that attenuation of leukocyte adherence during ischemia-reperfusion is evidence of the protective endothelial effect of Daflon 500 mg and its ability to control edema in clinical situation.

L66 ANSWER 8 OF 10 MEDLINE

ACCESSION NUMBER: 96112558 MEDLINE
DOCUMENT NUMBER: 96112558 PubMed ID: 8847003
TITLE: Review of the biology of Quercetin and related bioflavonoids.
AUTHOR: Formica J V; Regelson W
CORPORATE SOURCE: Department of Microbiology and Immunology, School of Medicine, Virginia Commonwealth University, Richmond 23298-0678, USA.
SOURCE: FOOD AND CHEMICAL TOXICOLOGY, (1995 Dec) 33 (12) 1061-80. Ref: 210
Journal code: 8207483. ISSN: 0278-6915.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961106
Last Updated on STN: 19961106
Entered Medline: 19961022

AB The French paradox is a dietary anomaly which has focused attention on the Mediterranean diet. Epidemiological studies revealed that this diet, replete in flavonoid-rich foods (Allium and Brassica vegetables, and red wine), correlated with the increased longevity and decreased incidence of cardiovascular disease seen in these populations. The most frequently studied flavonoid, quercetin, has been shown to have biological properties consistent with its sparing effect on the cardiovascular system. Quercetin and other flavonoids have been shown to modify eicosanoid biosynthesis (antiprostanoid and anti-inflammatory responses), protect low-density lipoprotein from oxidation (prevent atherosclerotic plaque formation), prevent platelet aggregation (antithrombic effects), and promote relaxation of cardiovascular smooth muscle (antihypertensive, antiarrhythmic effects). In addition, flavonoids have been shown to have antiviral and carcinostatic properties. However, flavonoids are poorly absorbed from the gut and are subject to degradation by intestinal micro-organisms. The amount of quercetin that remains biologically available may not be of sufficient concentration, theoretically, to explain the beneficial effects seen with the Mediterranean diet. The role of flavonoids may transcend their presence in food. The activity of flavonoids as inhibitors of reverse transcriptase suggests a place for these compounds in the control of retrovirus infections, such as acquired immunodeficiency syndrome (AIDS). In addition to specific effects, the broad-modulating effects of flavonoids as antioxidants, inhibitors of ubiquitous enzymes (ornithine carboxylase, protein kinase, calmodulin), and promoters of vasodilatation and platelet disaggregation can serve as starting material for drug development programmes.

L66 ANSWER 9 OF 10 MEDLINE
ACCESSION NUMBER: 94239647 MEDLINE
DOCUMENT NUMBER: 94239647 PubMed ID: 8183470
TITLE: Dietary flavonoids and risk of coronary heart disease.
AUTHOR: Anonymous
SOURCE: NUTRITION REVIEWS, (1994 Feb) 52 (2 Pt 1) 59-61. Ref: 12
Journal code: 0376405. ISSN: 0029-6643.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940621

Last Updated on STN: 19940621
Entered Medline: 19940610

L66 ANSWER 10 OF 10 MEDLINE
ACCESSION NUMBER: 91374952 MEDLINE
DOCUMENT NUMBER: 91374952 PubMed ID: 1654477
TITLE: [Leukotrienes and myocardial ischemia].
Leikotrieny i ishemiia miokarda.
AUTHOR: Moibenko A A; Kolchin Iu N; Kotsiuruba V N
SOURCE: KARDIOLOGIIA, (1991 May) 31 (5) 79-82. Ref: 92
Journal code: 0376351. ISSN: 0022-9040.
PUB. COUNTRY: USSR
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 19911108
Last Updated on STN: 19970203
Entered Medline: 19911021

FILE 'HOME' ENTERED AT 10:32:56 ON 22 MAY 2003